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Fox et al.

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(54) **METHOD OF CREATING INDUSTRIAL STREPTOMYCES WITH CAPABILITY TO GROW ON CELLULOSIC POLYSACCHARIDE SUBSTRATES**

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Related U.S. Application Data

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(51) **Int. Cl.**

C07H 21/04	(2006.01)
C12N 9/42	(2006.01)
C12N 9/24	(2006.01)
C12N 15/09	(2006.01)
C12N 15/74	(2006.01)
C12P 19/14	(2006.01)
C12P 19/02	(2006.01)
C12N 15/76	(2006.01)
C12N 15/52	(2006.01)

(52) **U.S. Cl.**

CPC ***C12N 15/76*** (2013.01); ***C12N 9/2434*** (2013.01); ***C12N 9/2437*** (2013.01); ***C12N 15/52*** (2013.01); ***C12P 19/02*** (2013.01); ***C12P 19/14*** (2013.01); ***C12Y 302/01004*** (2013.01); ***C12Y 302/01091*** (2013.01); ***C12Y 302/01176*** (2013.01); *C12P 2203/00* (2013.01)

(58) **Field of Classification Search**

CPC C12N 15/80; C12N 9/2437; C12N 9/2448; C12Y 302/01091; C12Y 302/01004

USPC 435/209, 254.11, 254.3, 320.1, 252.2; 536/23.2

See application file for complete search history.

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(Continued)

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(57) **ABSTRACT**

A heterologous gene cassette useful for creating *Streptomyces* species with enhanced capability of growing on a cellulosic polysaccharide substrate, wherein the cassette comprises at least two members of the following categories: a) a GH6 gene, b) an AA10 gene, c) a GH48 gene, d) a GH5 gene and e) either (i) a GH9 gene, (ii) a GH9 gene and a GH12 gene, or (iii) a GH12 gene is disclosed.

20 Claims, 27 Drawing Sheets
(12 of 27 Drawing Sheet(s) Filed in Color)

Specification includes a Sequence Listing.

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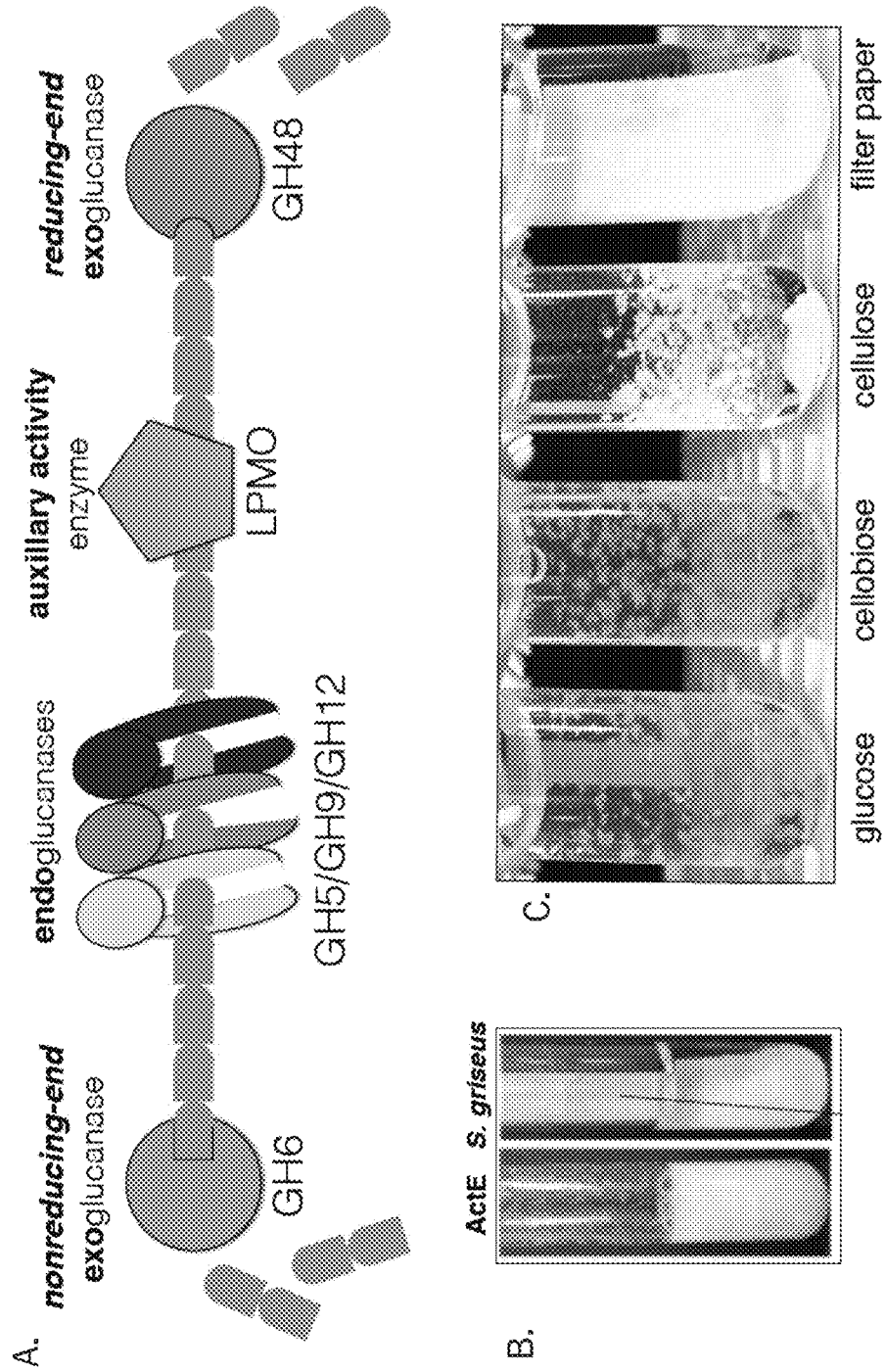
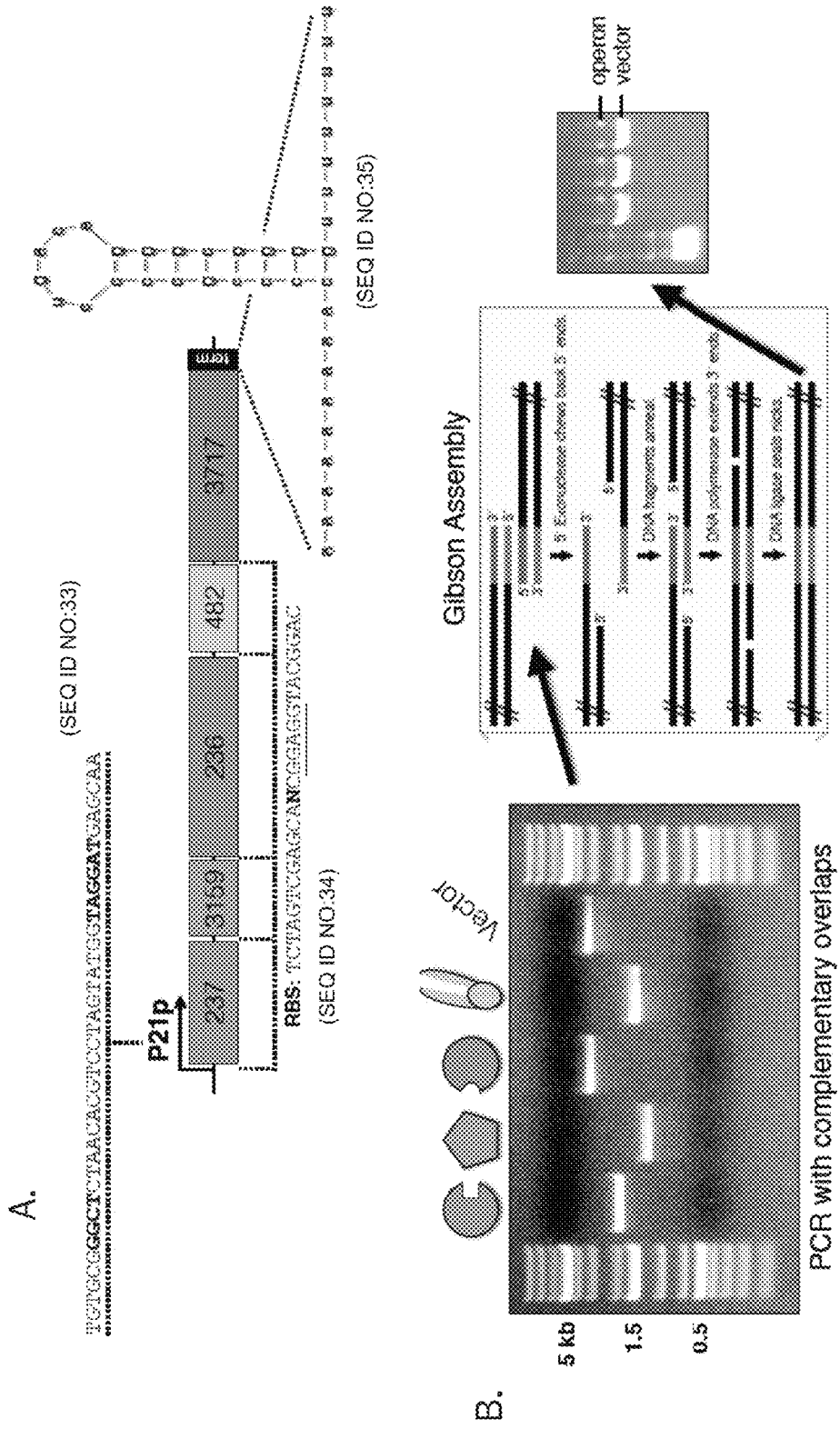

A.
nonreducing-end
exoglucanase
endoglucanases
auxillary activity
enzyme
reducing-end
exoglucanase
GH6
GH5/GH9/GH12
LPMO
GH48
B.
ActE S. griseus
C.
glucose
cellobiose
cellulose
filter paper

FIGS. 1A-1C


A.
(SEQ ID NO:33)
P21p
237
3139
236
482
3717
RBS
(SEQ ID NO:34)
(SEQ ID NO:35)
B.
Vector
Gibson Assembly
operon
vector
5 kb
1.5
0.5
PCR with complementary overlaps

FIGS. 2A-2B

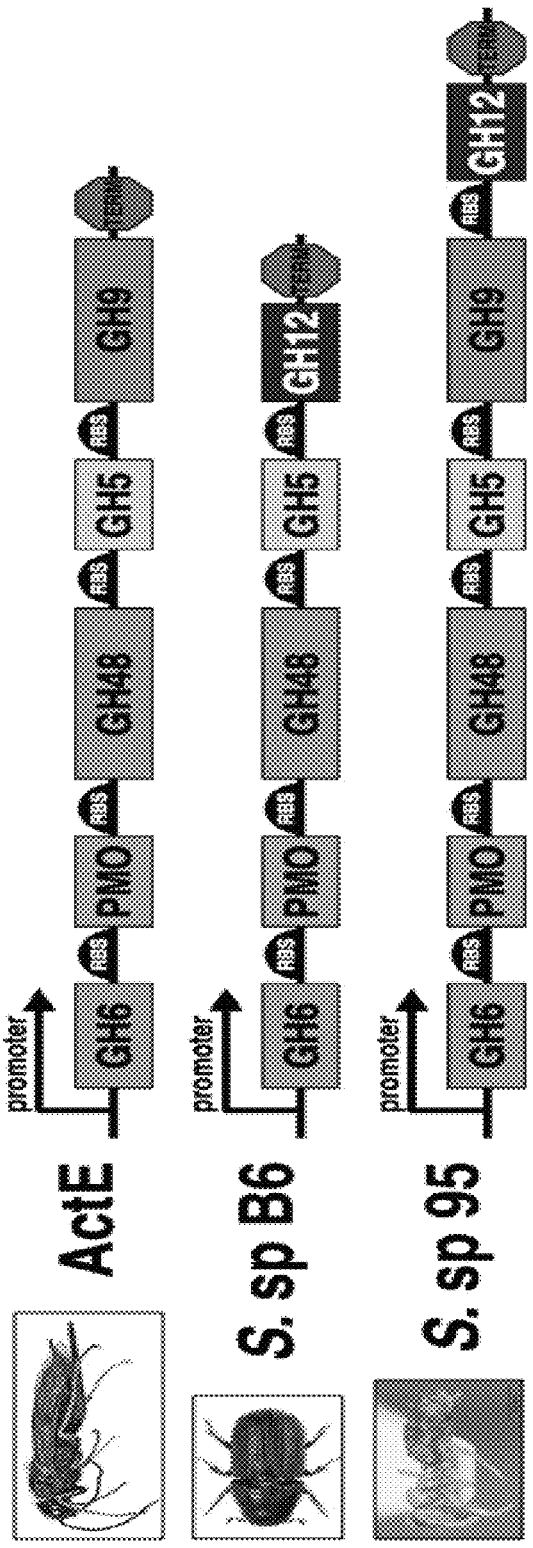

ActE
promoter
GH6
CBM
PMO
CBM
GH48
CBM
GH5
CBM
GH9
S. sp B6
promoter
GH6
CBM
PMO
CBM
GH48
CBM
GH5
CBM
GH12
S. sp 95
promoter
GH6
CBM
PMO
CBM
GH48
CBM
GH5
CBM
GH9
CBM
GH12

FIG. 3

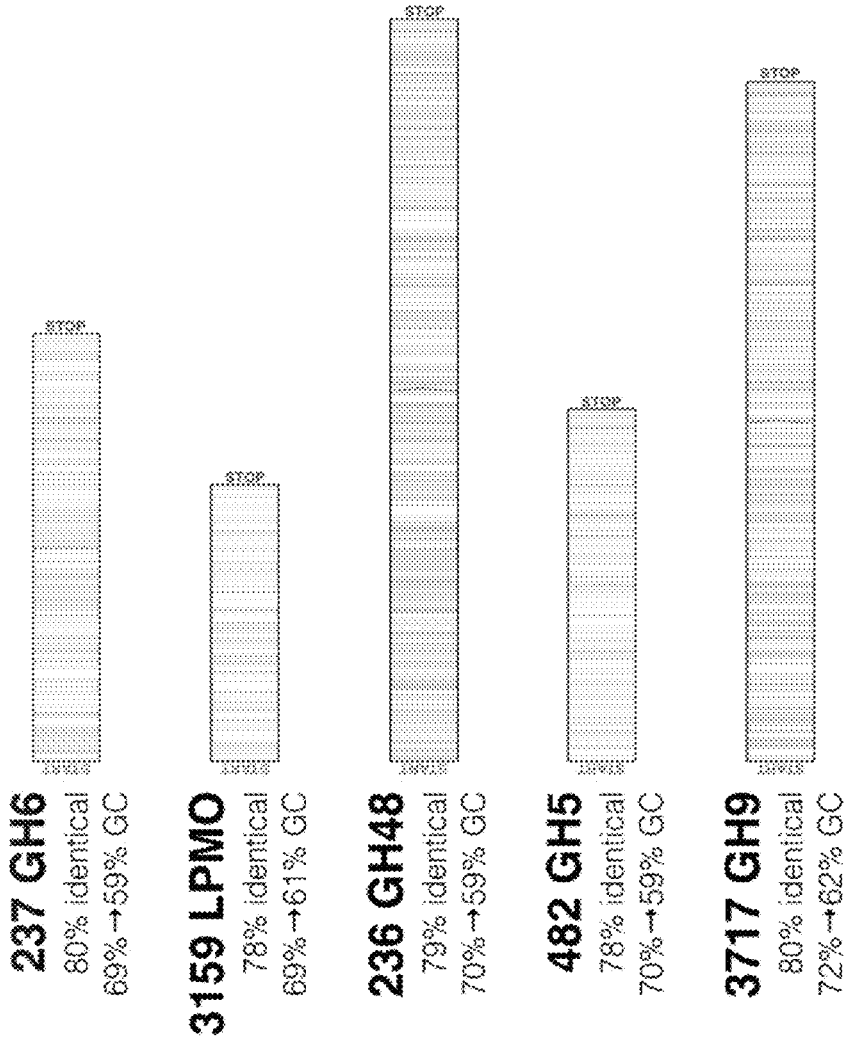

237 GH6
80% identical
69%→59% GC
3159 LPMO
78% identical
69%→61% GC
236 GH48
79% identical
70%→59% GC
482 GH5
78% identical
70%→59% GC
3717 GH9
80% identical
72%→62% GC

FIG. 4

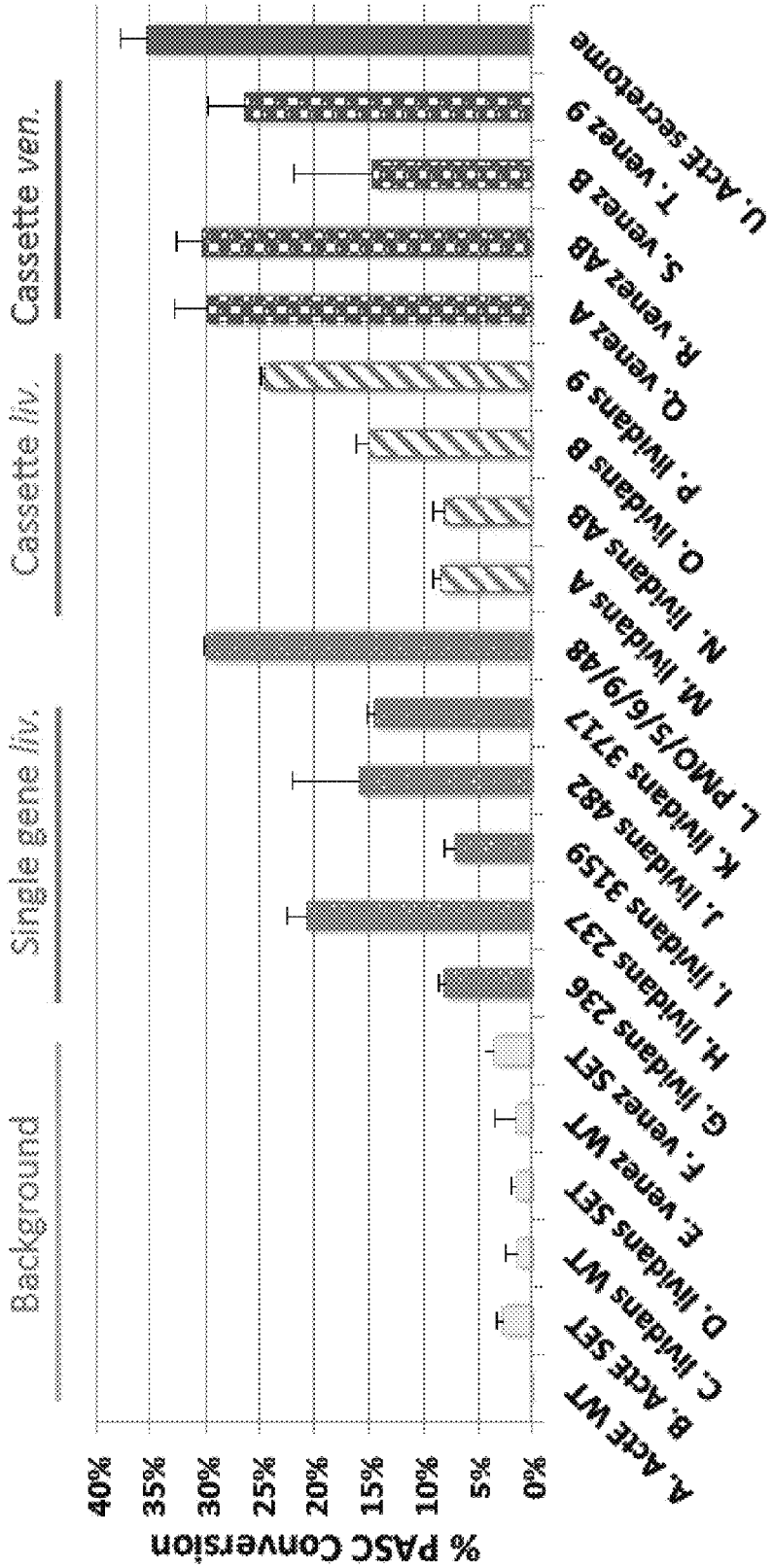

% PASC Conversion
40%
35%
30%
25%
20%
15%
10%
5%
0%
Background
Single gene liv.
Cassette liv.
Cassette ven.
A. AcfE WT
B. AcfE SET
C. lividans WT
D. lividans SET
E. venez WT
F. venez SET
G. lividans 236
H. lividans 237
I. lividans 3159
J. lividans 482
K. lividans 3717
L. PMO/5/6/9/48
M. lividans A
N. lividans AB
O. lividans B
P. lividans 9
Q. venez A
R. venez AB
S. venez B
T. venez 9
U. AcfE secretome

FIG. 5

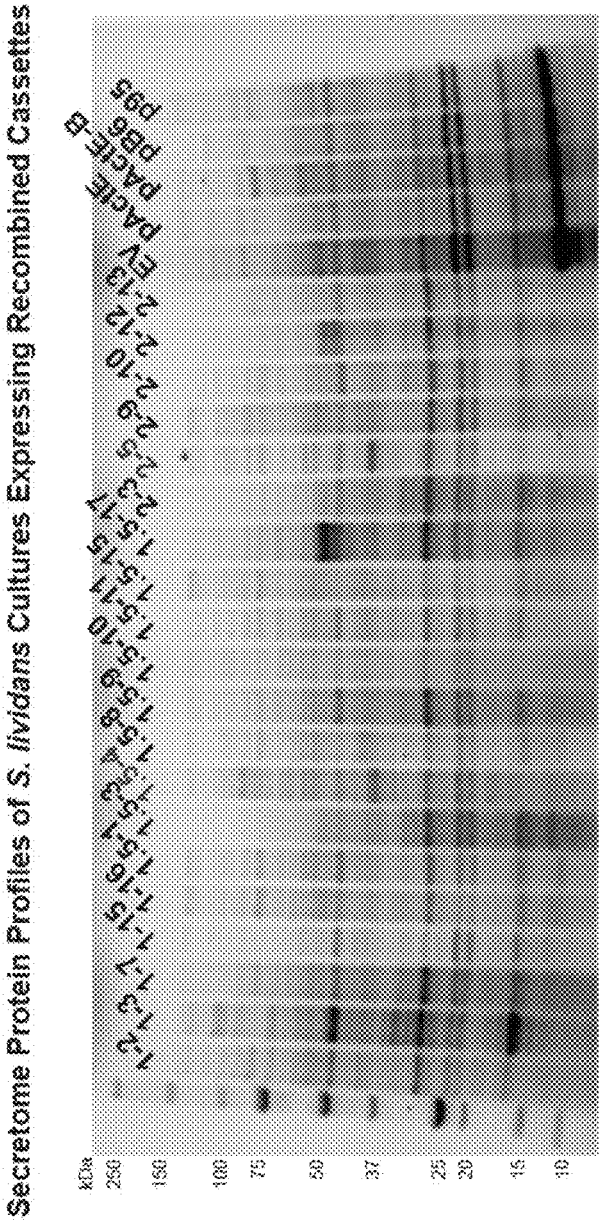

Secretome Protein Profiles of S. lividans Cultures Expressing Recombined Cassettes
kDa
250
150
100
75
50
37
25
20
15
10
pACTE-B
pBS

FIG. 6

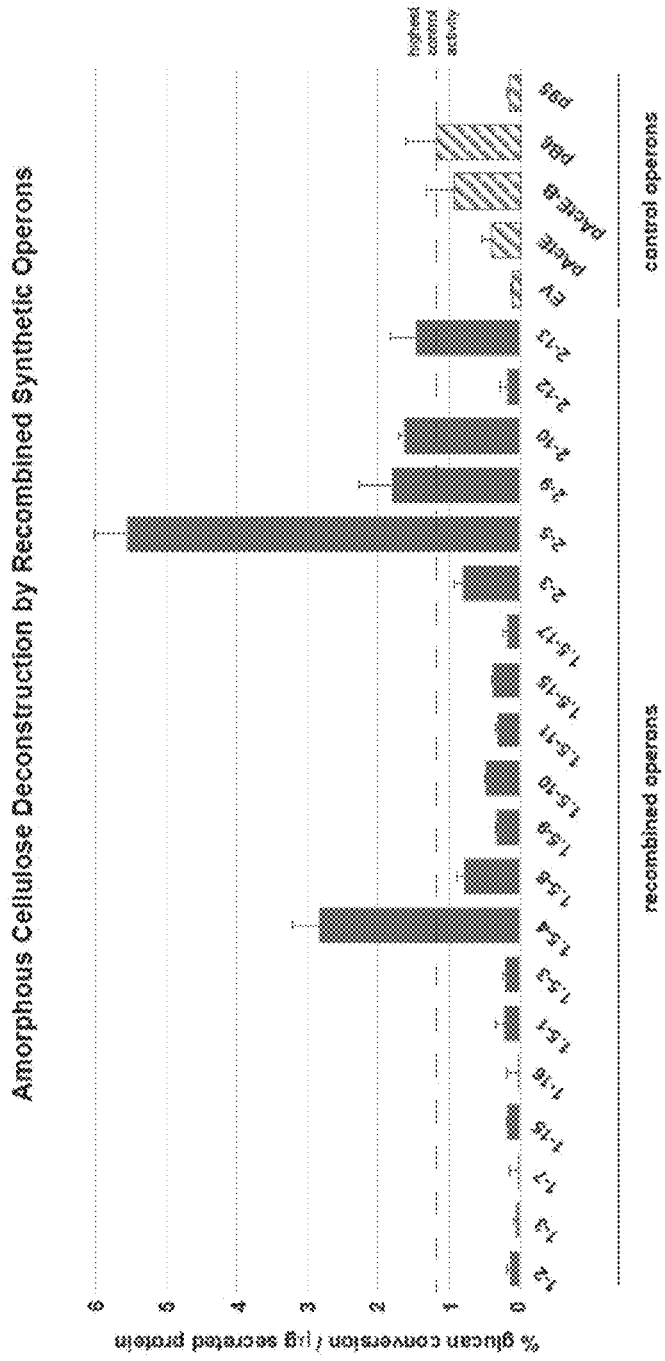

Amorphous Cellulose Deconstruction by Recombined Synthetic Operons
% glucan conversion / µg secreted protein
0
1
2
3
4
5
6
recombined operons
control operons
1-2
1-3
1-7
1-15
1-16
1-E1
1-E3
1-E4
1-E6
1-E8
1-E10
1-E11
1-E15
1-E17
2-3
2-5
2-9
2-10
2-12
2-13
EV
pAceE
pAceE-B
pBbE
pBbE-B

FIG. 7

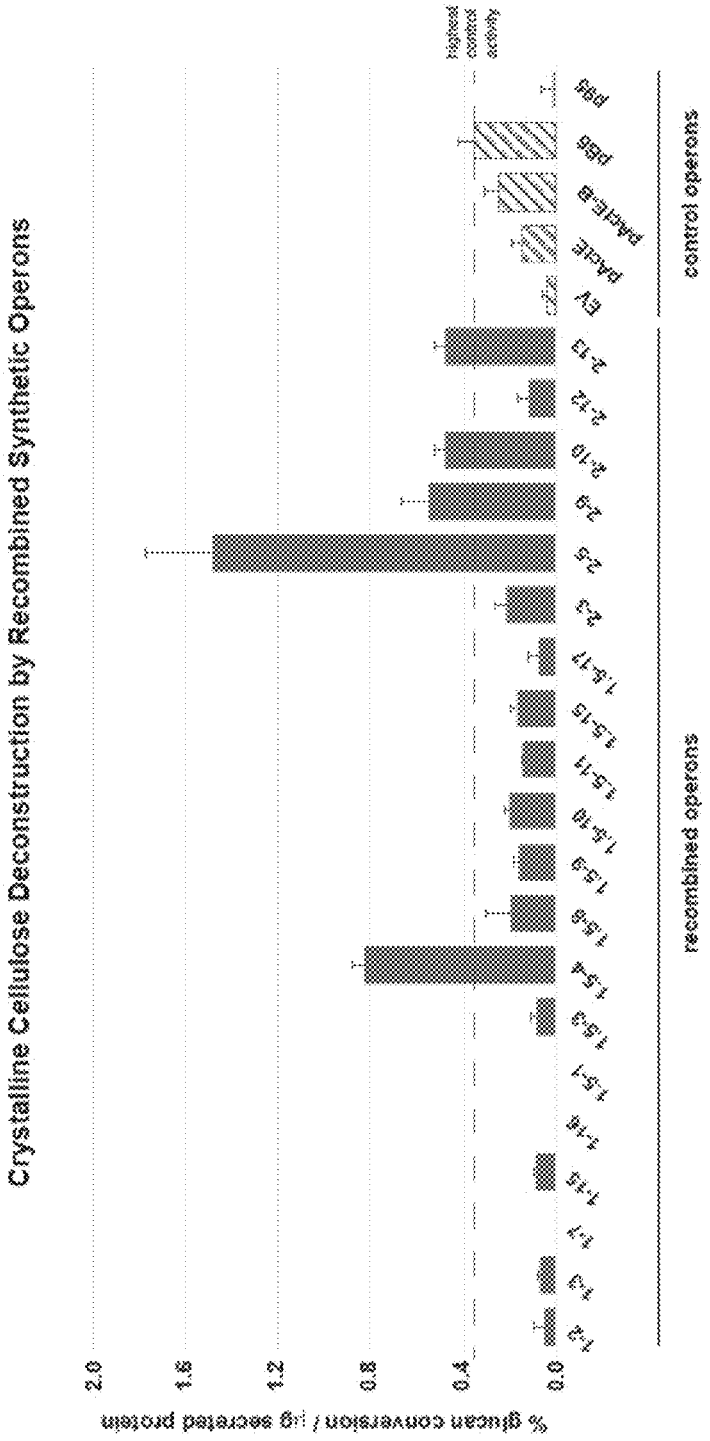

Crystalline Cellulose Deconstruction by Recombined Synthetic Operons
% glucan conversion / μg secreted protein
2.0
1.6
1.2
0.8
0.4
0.0
1-2
1-3
1-7
1-15
1-16
1-5-1
1-5-3
1-5-4
1-5-6
1-5-9
1-5-10
1-5-11
1-5-15
1-5-17
2-3
2-5
2-9
2-10
2-12
2-13
EV
pAcdE
pAcdE-B
pBS
pBA
recombined
acdE
recombined operons
control operons

FIG. 8

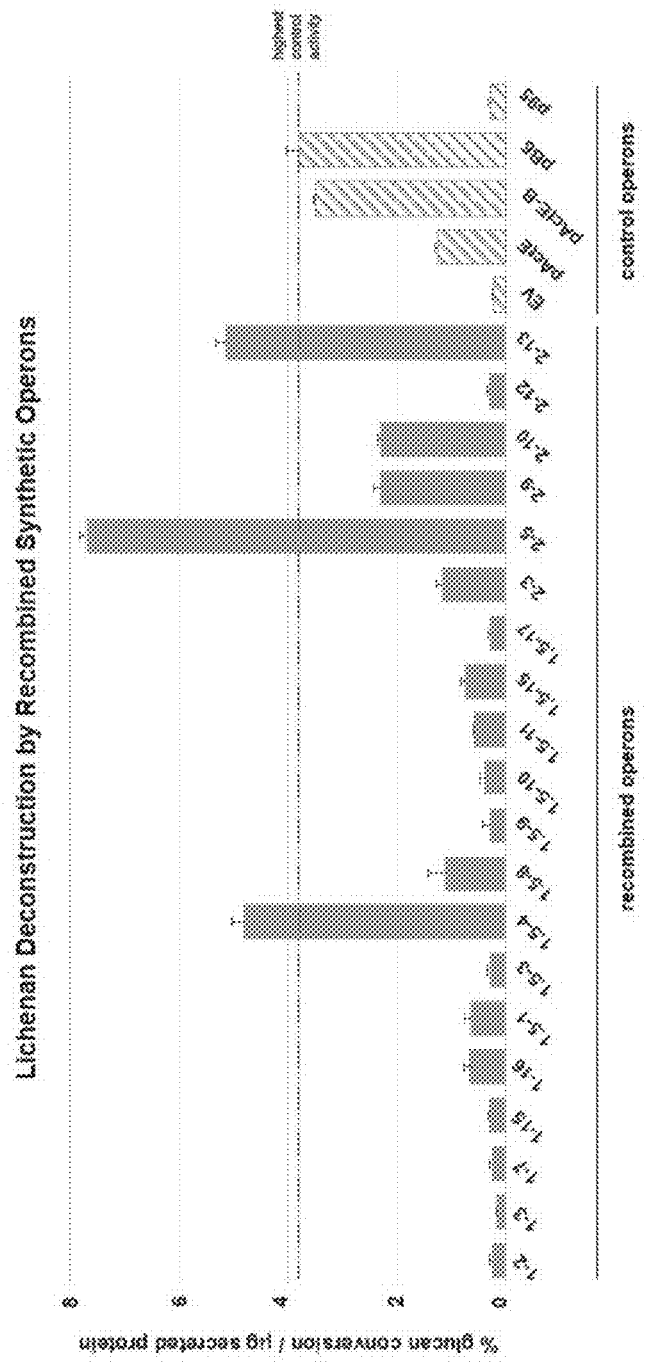

Lichenan Deconstruction by Recombined Synthetic Operons
% glucan conversion / µg secreted protein
0
2
4
6
8
control operons
recombined operons
EV
pAcetE
pAcetE-B
pBbs
1-2
1-3
1-7
1-13
1-15
1-5
1-3
1-4
1-8
1-9
1-10
1-11
1-15
1-17
2-3
2-5
2-9
2-10
2-12
2-13

FIG. 9

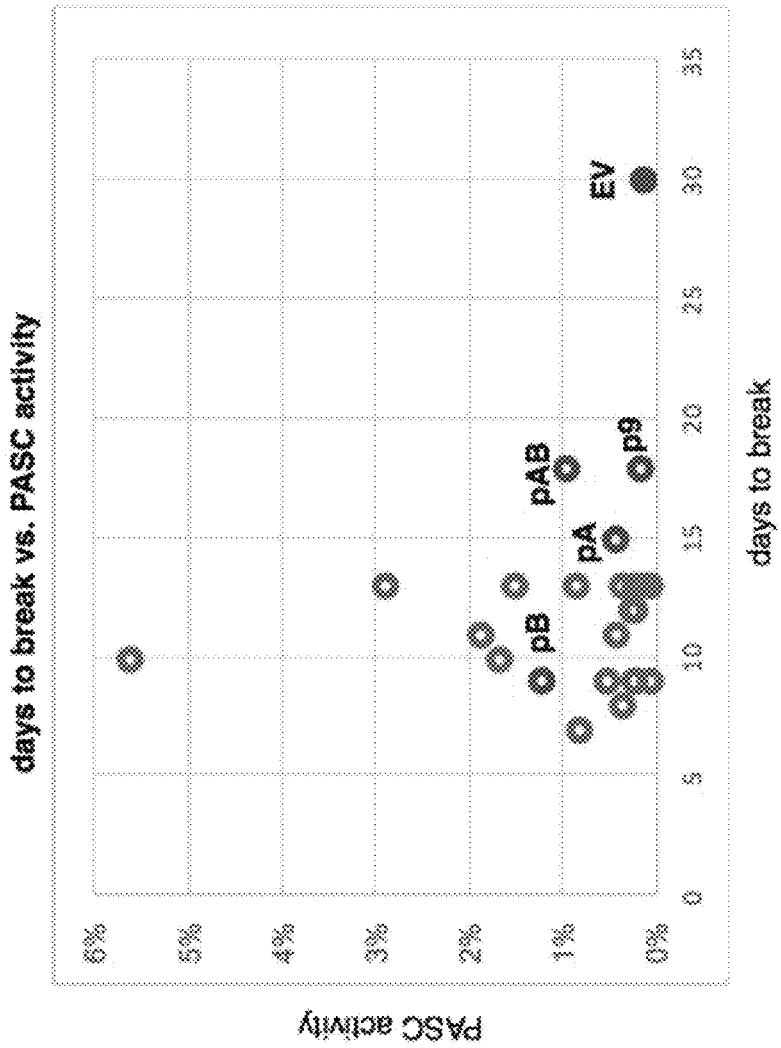
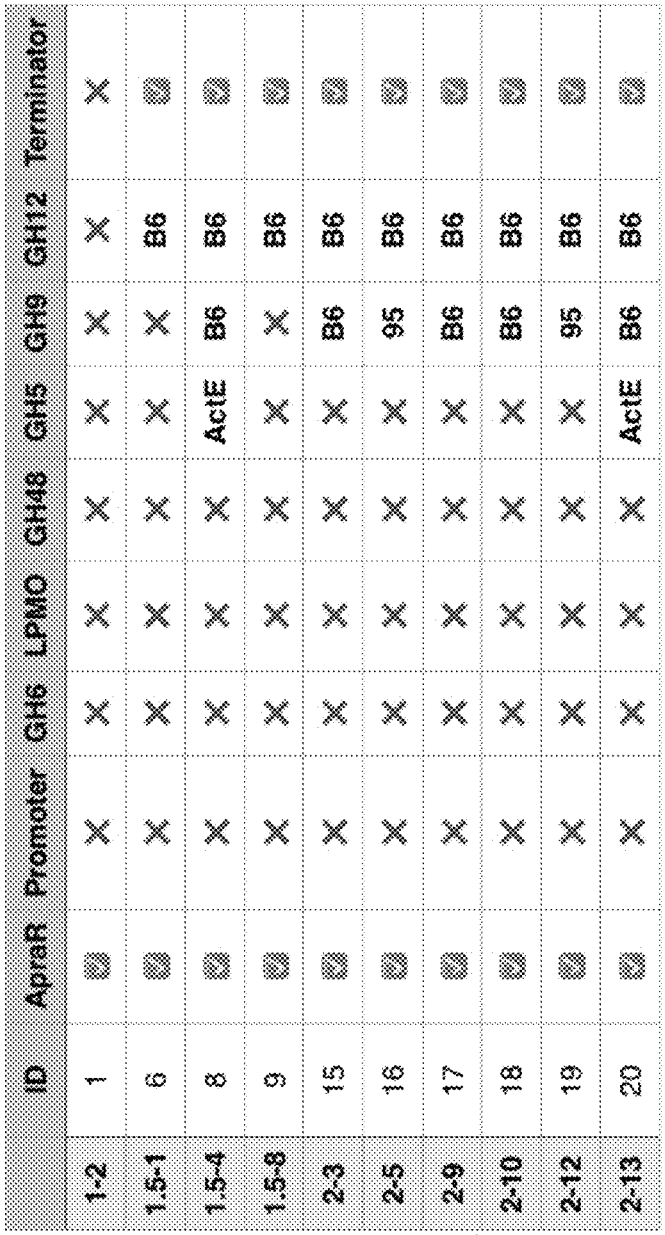

days to break vs. PASC activity
PASC activity
days to break
6%
5%
4%
3%
2%
1%
0%
0
5
10
15
20
25
30
35
EV
p9
pAB
pA
pB

FIG. 10



	ID	ApraR	Promoter	GH6	LPMO	GH48	GH5	GH9	GH12	Terminator
1-2	1		X	X	X	X	X	X	X	X
1.5-1	6		X	X	X	X	X	X	B6	
1.5-4	8		X	X	X	X	ActE	B6	B6	
1.5-8	9		X	X	X	X	X	X	B6	
2-3	15		X	X	X	X	X	B6	B6	
2-5	16		X	X	X	X	X	95	B6	
2-9	17		X	X	X	X	X	B6	B6	
2-10	18		X	X	X	X	X	B6	B6	
2-12	19		X	X	X	X	X	95	B6	
2-13	20		X	X	X	X	ActE	B6	B6	

FIG. 11

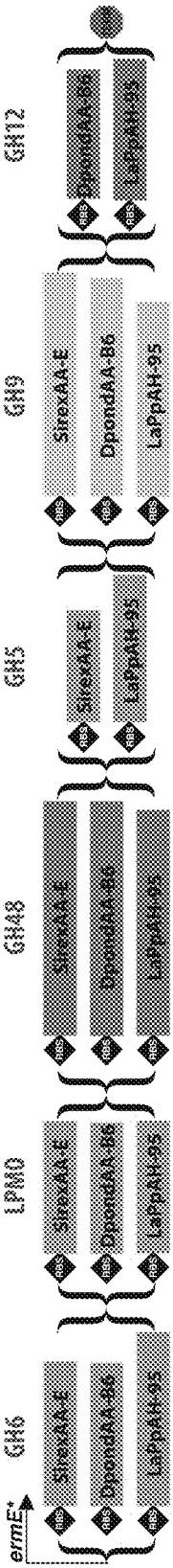

ermE*
GH6
SlroxAA-E
DpondAA-B6
LaPpAH-95
LPMO
SlroxAA-E
DpondAA-B6
LaPpAH-95
GH48
SlroxAA-E
DpondAA-B6
LaPpAH-95
GH5
SlroxAA-E
LaPpAH-95
GH9
SlroxAA-E
DpondAA-B6
LaPpAH-95
GH12
DpondAA-B6
LaPpAH-95

FIG. 12

Example 2 protein sequences

>95GH5 (SEQ ID NO:1)

MLHPLRTFRRAARTVAVATAALLLPLAGAHPASADAARAAAAGSGYWHTSGRQILDAANQ
PVRIAGINWFGFETANYVPHGLWSRDYKSMIDQMRSLGYNTIRLPYSDDIFAGTEPASIN
YSAGMNTDLAGLNSLQVMDRIVDHAGSFGMKVILDRHRPDSAGQSALWYTSAVPESTWLA
HLKSLAARYAGNDAVVGIDLHNEPHDPACWGCGDTTKDWRLAAQRGGNAALSANPDLLIF
VEGVQTVDGVSGWWGGNLMGVGQYPVELSVPHKVVYSAHDYATSVAQQPWFTDSSFPDNM
PGVWDKYWGYIFKQNIAPVWVGEFGTTLQSTTDQKWLKALADYLRPTSQYGADSFSWTFW
SWNPNSGDTGGILKDDWTSVDTVKDGYLASIKAPDFGNGGSGGDDTQAPTAPTGLAVT
GTTGTSVSLSWKAASDDTGVTAYDVYRGSTKAGTATGTTFTDTGVTSGTSYTYTVRARDA
AGNTSAPSASVTATTTGSGGNTGCKAVYTVNGDWGSGFGVDITVTNTGTAPATSWKLTWT
YGGSQKITNMWNASYTQSGASVTVTSTDYNGGLAAGAHTGFGFQGTPAAGAVPTVSCTLS
*

>95GH6 (SEQ ID NO:3)

MSTRGTIKQGLRRRLAAASALAMGAALAVAIPTTADAAAARVDNPYVGAKAYVNPDWSAK
AAAEPGGAAIADTPAFVWMDRIAAIGGTPGAMSLREHLDTALDQGANLFQVVIYDLPGRD
CAALASNGELGPTELDRYKSEYIDPISEILADPAYANLRIVTIIEPDSLPNIVTNAGGTA
GSTDACATMKANGNYEKGVGYALHTLGAIPNVYMYVDAAHAGWLGWDSNMVPAGVEFKKA
ATSEGATVDDVAGFIVNTANYSALKEPNFKITDSVMGTTVRQSKWVDWNYYTDELSFAQA
LRTQLVGQGFNSNIGMLIDTARNGWGGSDRPTSAGPLTSVDDYVNGGRVDRRIHAGNWCN
QSGAGIGERPTSAPEAGIDAYVWAKPPGESDGSSQAEDNDEGKGFDRMCDPTYEGNGRNG
NSKTGALPNSPVAGHWFSAQFQELVRMAYPPIDGSGENPGGGGDDDTQAPTAPTGLTSSA
KTSSSVSLSWTASSDNKAVTGYDVYRGGTKVGSTTTTSYTDTGLSASTAYSYTVKAKDAA
GNVSAASSALSVTTSAGGGTGTGSLKVQYKNNDNSPTDNQIRFGLQLVNTGSSAVDLSTV
KLRYWFTPESGSSTFGTACDYAVLGCGKLSLAVQSGGSAAGASHYLEVSFGSGSLAAGAS
TGEMQLRLNKSDWSNFNEADDYSHGTGTSFADASKIGVYTAGALSWGTAP*

>95GH9 (SEQ ID NO:4)

MRSFPLPALRRRSRRPGRPLGAVALALAVGAGLLLPLSLPAGAAAAPAFDYGEALQKSVL
FYEAQQSGKLPDTNRVSWRGDSALDDGKDAGLDLTGGWYDAGDHVKFGLPMAYSATMLAW
GGTEQRAAYEASGQLPHLRNNLRFVDDYLLKAHPSPNVLYGQVGNGGDDHKWWGPAEVMP
MKRPAYKIDASCPGSDLAGQTAAALASSSMVFSDSDPAYAAKLITHAKQLYTFADTYRGK
YSDCITDAQSYYNSWSGYNDELVWGAIWLYKATGDTAYLAKAESYYDNLSTEPQTTTRSY
RWTLSWDDTSYGAYVLLAQLTGKQKYIDDANRWLDWWTVGVNGQRVPYSPGGQAVLDSWG
SLRYAANTAFVALSYSDWLTGDATRKARYHDFAVRQIDYALGDNPRGSSYVVGFGENPPT
KPHHRTAHGSWTDQMTNPVETRHTLYGALVGGPSAPDDTYTDDRGNYVNNEVATDYNAAF
TGALARLYAEYGGSPLTDFPQPEEPDGPEMSVQASVNAAGANFTEVKAYLINRSAWPARA

FIG. 13

Example 2 protein sequences

LTDASVRYYFTLEPGVAPGDISFTTNYNQCGEVTGPTHLTGDVYYATVDCSDTDIAPAGQ
SAYRKEVQFRISSAGAWDPSNDWSYPSTATTPGGTPVDAPHMVLLEGSAPQWGTAPDGTD
PGPGPDPTTTPEPSPTPDPTDTPDPEPGACDVTYRVSQAWGTGFTADVTVKNTGPTPLDG
WQLAFDFQGAESVSNAWNATATQSGTRVTLKNAGHNGSVPAGGSASFGFQANGAPGADPH
SFTLNGKECG*

>95GH12 (SEQ ID NO:5)
MTGRPLPALAGAAAALVLAAASMLTGASSASASPVTDCTPWGTTELLGGEYLYQQNEWNS
DSEQCVGVDPDTGAWSVTTSSFNLPTNGAPATYPSSYKGCHWGACTSDSGLPLAVDELGS
VHTDWSTTQVGSGAYNVSMDVWFNSAPVTDDQPDGTELMIWMNHRGGVQPIGSRTATVQL
DGRTWDVWTGPGASGWKVISYVLQGGATELTGFDVKSLIDDGVGRGQIDPAHYLIDAEAG
FEIWQGGQGLGMKEFSFEASAGTDGGDGGDGPGGGTTGALKAQYKNNDSSATDNQIR
PGLQLVNTGSTAVDLSTVKLRYWFTPESGAAGFGTACDYAVVGCGNVTHTVKQAGTAAGA
SHYLEVGFTGGSLAPGASTGEIQLRFNKSDWSAFDEADDYSRAANTAFTDASKVGVYVNG
ALSSGTAP*

>95GH48 (SEQ ID NO:6)
MLAVGLAQGTAIARPASAQAGTGARAAAAGDDPYTQAFLTQYGKLKDAANGYFSPDGLPY
HSVETLMVEAPDHGHQTTSEAVSFWMWLEAAYGRVTGDWAPFNAAWAVAEKTIIPQHADQ
STSDSYNPSAPATYAPEHPLPSGYPSALDGTVPVGTDPLSAELASSYGTMDVYGMMWLMD
LDWVYGYGNKPGTGGESGPGAGASFINTYQRGAQESVWETVPQPTTDLFKYGGPNGYLDL
FVGDSSYAKQWKYTNAPDADARAVQAAYWAYRWASEQGKESQVAASVAKAAKMGDYLRYA
MFDKYFKRVGDCTDPNSCPAASGRDSQHYLLSWYYAWGGAAAGSGGGWAWRIGDGASHQG
YQNPLAAWALSNVPSLTPKSATARSDWSKSLTRQLEFLTWLQSSEGALAGGCTNSWEGSY
STPPAGTPTFYGMAYDWQPVYHDPASNNWFGFQAWGMERVAAYYYVTGNATAEAVLSKWV
AWASSETTIGSDGSFRFPSTLNWTGEPDTWNAASPGDNAGLHVSVVDYAMDVGVGAAYVK
TLTYYAAKSGDEDAAALAKALLDAMALNTTDKGISVPETRLDYNRFDDEVYIPSGWSGTM
PNGDPVRPGSTFISIRSWYKDDPDWPKVQAYLDGGDAPVFTYHRFWAQAALALAFAIYAE
LLVEGGGGEPGGDTEPPTAPGGLTVTATTKDSVSLSWSASTDNTAVTGYDVYRNGVLAGN
ATGRTFTDSGLAANTEYTYAVAARDAGGNTSALSDAVLAKTKTGGSTGTGAVKVQYKSTD
SSATDNQIRMGLQVVNTGSAPVDLSTVKVRYWFTADGGPSTFGTYCDYAALGSSTITHTV
VAVSSPKTGADRYLEVGFTGGAGTLAAGASTGEIQLRLNKSDWSNFNEADDYSRATNTAY
ADSSKVGAYVAGALAWGVEP*

>95LPMO (SEQ ID NO:7)
MARRRTQLASLAAVLATLLGGIAFTLLGQGSAQAHGVTMSPGSRTYYLCNLDAKTSTGSLD
PTNPACKAALAESGASSLYNWFAVLDSNAGGRGAGYVPDGTLCSAGDRSPYNFTGYNAAR

FIG. 13 (continued)

Example 2 protein sequences

GDWPRTHLTSGAKIEVDHSNWAAHPGEFRVVMSKPGYSPTTELGWDDLDLIQTVSNPPQV
GSPGTDGGHYYWDLTLPSGRSGDAVMFIQWVRSDSQENFFSCSDIVFDGGNGEVTGIRGS
GSTPDPDPTDPTPDPTDPTDPTDPHTGCMAVYNVTNSWSGGFQGSVEVMNHNTTALDGWA
VQWKPGTGTTVSSVWSGVLSTGSDGTLTVKNADYNRSIPPDGSVTFGFTATSTGNDFPVG
SIGCVSP*

>ActE236GH48 (SEQ ID NO:8)

MAALALPLGMTAAAGTEAQAAAVACSVDYTTSDWGSGFTTELTLTNRGSAAIDGWTLTYD
YAGNQQLTSGWSGTWSQSGKTVSVKNAAWNGAIAAGAAVTTGAQFTYSGANTAPTTFAVN
GTVCAGAHQPPIAVLTSPAAGAVFSAGDPVPLAATAAAADGATISKVEFYDDTTLLGTDT
TSPYSYEAGQLAAGSHSVVARAYDSLGASADSPPAGITVVTGPAVVVSPAQLGVQQGRSG
TFDVSLSTAPAADVTVTAARSAGNTGLSVTGGSTLTFTPANWSTPQKVTVTADGSGTGAA
TFTVTAPGHGKAEVTVTQLAAAKEYDARFLDLYGKITDPANGYFSPEGIPYHSVETLIVE
APDHGHETTSEAYSYLIWLQAMYGKITGDWTKFNGAWDTMETYMIPTHADQPTNSFYDAS
KPATYAPEHDTPNEYPAVLDGSASSGSDPIAAELKSAYGTDDIYGMHHWIQDVDNVYGYGN
APGTCAAGPTQAGPSYINTFQRGSQESVWETVTHPTCDNFTYGGANGYLDLFTGDSSYAK
QWKFTNAPDADARAVQAAYWADVWAKEQGKAGEVADTVGKAAKMGDYLRYSMFDKYFKKI
GDCVGPTTCPAGSGKDSAHYLMSWYYAWGGATDTSAGWSWRIGSSHAHGGYQNPMAAYAL
SSVADLKPKSATGAQDWAKSLDRQLDFYQWLQSDEGAIAGGATNSWKGSYAQPPAGTPTF
YGMYYDEKPVYHDPPSNQWFGFQAWSMERVAEYYHESGDAQAKAVLDKWVDWALSETTVN
PDGTYLMPSTLQWSGAPDTWNASNPGANAQLHVTVADYTDDVGVAGAVARTLTYYAAKSG
DTEAEATAEALLDGMWQHHQDDAGVAVPETRADYNRFDDPVVVPGGWTGAMPNGDTVDED
STFLSIRSFYKDDPNWPQVQAYLDGGAAPVFTYHRFWAQADIALALGAYADLLE*

>ActE237GH6 (SEQ ID NO:9)

MSRTSRTTLRRSRTALMAAGALVAAAAGSAAAAAPFGATAAAAAGCTVDYKIQNQWNGGL
TASVSVTNNGDAISGWQLQWSFAGGEQVSQGWNATVSQSGSAVTAKDAGYNAALATGASA
SFGFNATGNGNSVVPATFKLNGVTCNGGTTGPTDPTDPTDPTDPTDPPAGNRVDNPVQGA
KVYVNPEWSANAAAEPGGDRIADQPTGVWLDRIAAIEGANGSMGLRDHLDEALTQKGSGE
LVVQVVIYNLPGRDCAALASNGELGPTEIGRYKTEYIDPIAEILGDPKYAGLRIVTTVEI
DSLPNLVTNAGGRPTATPACDVMKANGNYVKGVGYALNKLGDAPNVYNYIDAGHHGWIGW
DDNFGASAEIFHEAATAEGATVNDVHGFITNTANYSALKEENFSIDDAVNGTSVRQSKAV
DWNRYTDELSFAQAFRNELVSVGFNSGIGMLIDTSRNGWGGANRPSGPGANTSVDTYVDG
GRYDRRIHLGNWCNQAGAGLGERPQAAPEPGIDAYVWMKPPGESDGSSSETPNDEGKGFD
RMCDPTYTGNARNNNNMSGALGGAPVSGKWFSAQFQELMKNAYPAL*

>ActE3159LPMO (SEQ ID NO:10)

FIG. 13 (continued)

Example 2 protein sequences

MARRSRLISLAAVLATLLGALGLTALWPGKAEAHGVAMTPGSRTYLCQLDALSGTGALNP
TNPACRDALSQSGANALYNWFAVLDSNAGGRGAGYYPDGSLCSAGDRSPYDFSAYNAARA
DWPRTHLTSGATLKVQYSNWAAHPGDFRVYLTKPGWAPTSELAWDDLQLVQTVSNPPQQG
GAGTNGGHYYWDLALPSGRSGDALMFIQWNVRSDSQENFFSCSDIVFDGGNGEVTGIGGTG
TPTPTPTPTPTPTPTPDPEHSGSCMAVYNVVSSWAGGFQASVEVMNHGTEPRNGWAVQWKP
GSGTQINSVWNGSLSTGSDGTVTVRDVDHNRVIAPDGSVTFGFTATSTGNDYPAGTIGCV
TS*

>ActE3717GH9 (SEQ ID NO:11)
MWCHPYLRLRTSGRKVSSVNALPPPARPAPVRPRSRYGRRVLGMSAAALLCAGALAVPGT
AMADDAEPGPGPEQITNGDFATGTSAPWWWTPNASAAVSEGRLCVEVPAGTANAWDVIVG
QWDVPIVAGESYELSYTARSTVPLTVQTRVQEAVEPYTTVLATADPVGAEDTRVARTFTA
SVDQPAASVQLQIGGGERATTFCLDDVSLRGGAEPPVVVPDTGSPVRVNQVGYLPRGPKS
GTVVTDAEAPLTWTVKAEDGSTAATGTTVPRGEDPSSRRRVHTFDFGDLTTAGDGVTVEV
DGEVSEPFSIRGDLYDSLRSDALAYFYHWRSGIEIDADLVGEQYARPAGHIGVAPNKGDT
DVPCRPGVCDYRLDVSGGWYDAGDHGKYVVNGGISVAQLMATYERTLTAPDAESAELGDG
ALRVPERDNGVPDILDEARWEMDFLIKMQVPAGEQLAGMVHHKMHDAEWTGLPMKPHLDP
QQRELHPPSTAATLNLAAATAAQCARLYAPFDADFADRCLRAAETAWDAAKRHPDVLADPN
DGIGGGAYNDDDVSDEFYWAAAELFTTTGKDIYRQAVLSSAWHGDAGAVFPAGGGISWGS
TAGLGVLTLATVPNALTSDQLAQVRTVVTEGADRYAAQSREQAYGLPYAPRGEDYVWGSN
SQVLNNMVVLATAHDLTGDAAYQDAVLRGADYLLGRNPLNQSYVTGYGERDSHNQHHRFW
AHQNDPSLPNPAPGSIAGGPNLTAIASGDPVAAEKLSGCAPAMCYVDDIGSWATMEITIN
WNAPLAFIASYLDDAGEGGQTAAARTCQVTYSSHPWNSGSTVTVRVENTGSDPVSPWALT
WLLPGEQRLSHTWSAEFDQHGRTVSARPLSWNRTLAPGAAVDFGFNTSAAGSSPEPGAFK
LNGRACSAG*

>ActeE482GH5 (SEQ ID NO:12)
MKRFLALLATCATVLGLTALTGPQAVAAAGCTADYTITSQWQGGFQAAVKVTNLGTPVTG
WKLTFTLPDAGQKVVQGWNAAWSQSGSAVTAAGADWNGTLATGASAEAGFVGSFTGANPP
PTAFALNGVACTGSTGEPPAGSDGGTPVDVNGQLHVCGVNLCNQYDRPVQLRGMSTHGIQ
WFDACYDAASLDALANDWKSDLLRIAMYVQEDGYETDPAGFTRRVNDLVDMAEARGMYAL
IDFHTLTPGDPNVNLDRAKTFFASVAARNAGKKNVIYEIANEPNGVTWTAVKSYAEQVIP
VIRAADPDAVVIVGTRGWSSLGVSDGSDESEVVNSPVNATNIMYAFHFYAASHKDAYRST
LSRAAARLPLFVTEFGTVSATGGGAMDRASTTAWLDLLDQLKISYANWTYSDAPESSAAF
RPGTCGGGDYSGSGVLTESGALLKNRISTPDSFPTG*

>B6GH6 (SEQ ID NO:13)

FIG. 13 (continued)

Example 2 protein sequences

MSRTSRTTLRRSRTALIAAGALVAAAAGSAAAAAPFAASAAAATGCTVDYKIENQWNGGL
TAAVNVTNNGAPVTSWQLQWTFNGGEQVSQGWNATISQSGSAVTAKDAGYNGTLATGASA
SFGFNATGNGNSTVPATFKLNGVTCNGDTTGPTDPTDPTDPPAGNRVDNPYQGAKVY
VNPEWSANAAAEPGGSRVANQPTGVWLDRIAAIEGANGSMGLREHLDEALTQKGSGELVV
QLVIYDLPGRDCAALASNGELGPTEIGRYKTEYIDPIAAIVADPKYAGLRIVTTVEIDSL
PNLVTNAGGRETATPACDVMKAWGNYVKGVGYALNKLGDAPNVYNYIDAGHHGWIGWDDN
FGASAQIFHEAATAEGATVNDVHGFITNTANYSALKEQNFSINDSVNGTSVRESKWVDWN
RYTDELSFAQAFRNELVSVGFNSGIGMLIDTSRNGWGGSARPSGPGATTSVDTYVDGGRY
DRRIHLGNWCNQAGAGLGERPTAAPEPGIDAYVWMKPPGESDGSSSEIPNDEGKGFDRMC
DPTYTGNPRNNNNPSGALGGAPVSGKWFSAQFQELMKNAYPAL*

>B6GH9 (SEQ ID NO:14)
MNALPPPARPAPVRSRSRYGRRALGISAAALLCAGALAVPGTALADDAAPGPEQITNGDF
SAGTAPWWTPNASAAVSEGRLCVEVPAGTAEAWDVIVGQNDIPIVAGESYELSYTARST
VPLTVQTRVQEAVEPYGTVLATADPVGTEDTQVTRTFTASVDQPAASVQLQIGGGERATT
FCLDDVSLRGGAEPPVYVPDTGSPVRVNQVGYLPRGVKSGTVVTDAEAPLTWTVKAGDGS
TAATGTTVPRGEDPSSRQRVHTFDFGGLTTPGDGYTVEVDGEVSEPFSIRGDLYDGLRSD
ALAYFYHWRSGIEIDADLVGEEYARPAGHIGVAPNKGDTDVPCKPGVCDYRLDVSGGWYD
AGDHGKYVVNGGISVAQLMSTYERTLTADNAESAQLDDGALRVFERGNGVPDILDEARWE
MDFLIKMQVPAGEPLAGMVHHKMHDAEWTGLPMKPHLDPQQRELHAPSTAATLNLAATAA
QCARLYAPYDEDFADRCLRAAETAWDAAKRHPDVFADPNDGVGGGTYDDNDVSDEFYWAA
AELFITTGKDTYRQEVLSSDLHGDADAVFPAGGGLSWGATAGLGALTLATVPNNLTTDQL
DGVRATVTTAADRYAAQSRAQAYGLPYAPRGTDYVWGSWSQVLNNMVVLAVAHDLTGEAA
YQDAVLRGADYLFGRNPLNQSYVTGYGERDSHNQHHRFWAHQYDSSLPNPAPGSVAGGPN
LTAAGSGDPVAAEKLSGCAPAMCYIDDIGSWSTNEITVNWNAPLAFIASYLDDAGDGGQT
TASRTCEVTYSSHPWSGGSTVSVRVENTGSAPVEPWSLTWLLPGEQKLSHTWSAEFEQHG
RTVSARPLAWNRTLAPGAAVDFGFNTSATGAAADPGTFFKLNGRACASG*

>B6GH12 (SEQ ID NO:15)
MKSLIASLRSAGTAVTASLVALATCAALGALAAPAQAADSICGQYGTTVIQDRYVYQNNR
WGTTDAQCVDVTDDGFTVTRADGSVPTNGAPKSYPSVYNGCHYTNCSPGTELPKRLDSIS
SAPTAITYTYVDGAVYDAAYDIWLDPQPKKDGVNRTEIMIWFNRVGPIQPVGSQTGTATV
AGRGWEVWTGNNGGNDVISFVSPSAISSWSFDVMDFVDATVARGMAQNSWYLTSVQAGFE
PWQNGAGLAVSSFSSSSVLTGGGSEGPGEPGTPADGPCAVSYTANAWTDGFTADVKVTNTG
TVPVSGWRLGFTLPQGQTVTQAWNATVTPSSGAVTATGAAFNAEIAAGASQSFGFQGTHS
GTFTKPDRFTLNGAVCTVG*

FIG. 13 (continued)

Example 2 protein sequences

>B6GH48 (SEQ ID NO:16)
MAALALPLGMTAAAGTPAQAAAVACSVDYKANDWGSGFTTELTLTNRGSGAIDGWTLTYD
YAGNQQLTSGWSGVWSQSGKTVTVKNADWNGTVAAGQAVTAGAQFTYSGTNTDPTAFAVN
GTVCAGAHQPPIAVLTSPAAGAVFTAGDPVPLAATAAAADGATISKVEFYDNTTLLGTDT
TSPYSYTAQGLSAGSHSVYARAYDSLGASAESPPAGITVAAGPAVVATPAQLGVQQGKSG
TFNVSLSTAPASNVTATVARTAGNTGLSVTGGASLTFTPANWSTPQKVTVSADGSGTGAA
TFTVSAPGHGKAEVTVTQLAGAKEYDARFLDLYGKVTDPANGYFSPEGIPYHSVETLIVE
APDHGHETTSEAYSYLIWLQAMYGKITGDWTRFNGAWDTMETYMIPTHADQPTNAYYDAS
KPATYAPEHDTPNEYPAVLDGSVSSGSDPIAAELKSAYGTDDIYGMHWIQDVDNVYGYGN
SPGTCAAGPTQTGPSYINTFQRGPQESVWETVTHPTCDNFTYGGANGYLDLFTGDSSYAK
QWKFTNAPDADARAVQAAYWADVWAKEQGKSADVAGTVGKAAKMGDYLRYSMFDKYFKKI
GDCVGPTTCPAGSGKDSSHYLMSWYYAWGGATDTSAGWAWRIGSSHAHGGYQNPMAAYAL
SSVADLKPKSATGQQDWAKSLDRQLDFYQWLQSDEGAIAGGATNSWKGGYAQPPAGTPTF
HGMYYDEKPVYHDPPSNQWFGFQAWSMERVAEYYHESGDAQAKAVLDKWVDWALSETTVN
PDGTYLMPSTLQWSGAPDTWNASNPGSNAGLHVTVADYTNDVGVAGAYARTLTYYAAKSG
DADAKATAEALLDGMWQHYQDDAGVAVPETRADYNRFDDPVYVPGGWTGAMPNGDTVDQD
STFVSIRSFYQDDPNWPKVQAYLDGGAAPVFTYHRFWAQADIALALGAYADLLE*

>B6LPMO (SEQ ID NO:17)
MAGRSRLISLAAVLATLLGALGLTALWQGKAEAHGVAMMPGSRTYLCQVDALSGTGALNP
TNPACRDALSKSGANALYNWFAVLDSNAGGRGAGYVPDGTLCSAGDRSPYDFSAYNAARA
DWPKTHLTSGAGIQLQYSNWAAHPGDFRVYVTKPSWSPTSALGWNDLQLVQTVSNPPQQG
SPGANGGHYYWDLTLPSGRSGDALMFIQWVRSDSQENFFSCSDIVFDGGKGEVTGIGGSG
NGTPTPTPTPTPTPTDPEHSGSCMAVYNVESSWNGGFQASVEVMNHGTEPRNGWAVQWKPGT
GTQINSVWNGTLSTGSDGTVTVRNVDHNRVIAPDGSVTFGFTANSTGNDFPAGTIGCVTS
*

FIG. 13 (continued)

Example 2 DNA sequences

>ActE GH6 (SEQ ID NO:2)

ATGAGTCGTACGTCCCGCACCACACTGCGTCGCAGTCGGACGGCGCTGATGGCAGCAGGTGCACTCGTCGCGGCAGCCGCAGGGAGCGCAGCAGCAGCCGCTCCGTT
CGGAGCAACGGCAGCGGCCGCAGCAGGATGCACGGTCGACTATAAGATCCAGAACCAGTGGAATGGCGGTCTGACAGCATCAGTCTCCGTGACAAACAACGGGGACG
CCATCTCAGGTTGGCAGCTGCAGTGGAGCTTCGCAGGCGGAGAGCAGGTCAGCCAGGGTTGGAATGCCACAGTATCCCAGAGCGGATCGGCAGTCACGGCCAAGGAC
GCAGGTTATAACGCAGCGCTCGGCCACCGGAGCCTCGGCCAGCTTCGGTTTCAATGCAACGGGCAATGGAAACAGCGTCGTTCCGGCAACCTTCAAGTTGAATGGTGT
AACCTGCAACGGGGGTACGACAGGACCCGACGACCCCACCCGACCCTCCGGCAGGTAATCGAGTGGACAACCCTTACCAGG
GAGCAAAGGTTTATGTCAACCCGGAATGGTCCGCCAACGCCGCAGCCGAACCCGGCGGTGACCGCATAGCGGACCAGGTGTCTGGTTGGATCGTATAGCG
GCCATCGAGGGGGCCAATGGAAGTATGGGCCTTCGCGACCACCTGGACGAAGCGTTGACGCAAAAAGGAAGCGGAGAGCTGGTGGTCCAAGTGGTCATCTACAATCT
CCCAGGTCGTGACTGTGCCGCACTGGCCTCGAACGGAGAACTCGGGCCGACCGAGATCGGACGCTACAAAAACAGAATATATCGATCCGATAGCGGAGATCCTGGGTG
ACCCGAAGTACGCAGGGCTCCGGATCGTCGACGACGGTAGAAATCGATAGTCTGCCGAATTTGGTCACTAATGCCGGAGGACGTCCAACGGCAACACCGGCGTGCGAC
GTCATGAAAGCCAACGGTAATTATGTGAAGGGTGTCGGATATGCACTGAACAAGCTCGGGGATGCGCCGAATGTGTGTACAATTATATCGACGCAGGTCATCACGATG
GATCGGATGGGATGACAACTTCGGCGCCTCTGCAGAGATCTTCCACGAAGCGGCCACCGCAGAGGGGGCAACGGTCCATGGTTTCATCACCAACACAG
CGAACTACTCAGCGCTGAAGGAAGAAGAACTTCTCGATCGATGATAAACGGCACCAGCGTCCGCCAGTCTAAGTGGGTGGACTGGAATCGATACACAGACGAG
CTCAGCTTCGCCCAGGCATTCCGCAATGAACTCGTGAGTGTGGGTTTCAACTCCGGTATCGGAATGCTGATTGACACGTCGCGGAACGGTTGGGGCGGAGCAAATCG
TCCGTCGGGCCCGGGTGCCAATACATCCGTCGACACGTATGTAGACGGAGGCCGCTACGATCGACGGATCCATCTCGGTAACTGGTGTAATCAGGCAGGTGCGGGAC
TCGGTGAACGCCCGCAGGCTGCGCCAGAACCGGGCATCGACGCCTACGTGTGGATGAAGCCCCCCGGGAGAGAGTGACGGATCCAGCTCCGAAATTCCGAACGATGAG
GGCAAGGGATTCGACCGTATGTGCGACCCGACATACACGGGCAACGCACGGAATAACAACAATATGAGTGGCGCGCTGGGAGGTGCCCCCGTCTCGGGAAAGTGGTT
CAGTGCCCAATTCCAAGAGCTGATGAAAAATGCGTATCCGGCATTGTGA

>ActE LPMO (SEQ ID NO:18)

ATGGCCCGCCGCAGCCGACTGATCTCACTTGCAGCGGTCTTGGCAACCTTGCTTGGCGCATTGGGTCTGACGGCCCTGTGGCCGGGCAAGGCCGAAGCGCATGGTGT
CGCAATGACACCCGGTAGCCGGACCTACCTGTGCCAGTTGGACGCCCTCAGTGGGACAGGTGCGCTTAACCCGACGAACCCCGCCTGTCGAGATGCACTGAGCCAGT
CGGGTGCCAACGCCCTCTATAATTGGTTCGCAGTACTGGACTCTAACGCCGGCGGAAGGGGAGCGGGCTATGTGCCAGACGGATCCCTGTGCAGTGCAGGGGACCGC
TCCCCCTACGATTTCTCAGCATACAATGCGGCACGTGCCGACTGGCCGCGGACCCACCTGACGAGCGGCGCCACACTCAAGGTCCAATATTCGAACTGGGCAGCACA
CCCCGGTGACTTCCGTGTGTATCTGACAAAACCCGGATGGGCGCCGACCTCAGAGCTGGCCTGGGATGACCTTCAGCTCGTGCAAACCGTCTCGAATCCGCCCCAAC
AAGGAGGAGCAGGCACCAACGGGGGGCACTACTATTGGGATCTGGCGCTGCCGAGCGGGAGAAGTGGAGACGCATTGATGTTCATCCAGTGGGTGCGTTCGGATAGC
CAGGAGAACTTCTTCTCGTGTAGTATATAGTGTTCGACGGAGGTAATGGGGGAGGTAACTGGAATCGGGGGAACGGGAACACCCACACCGACGCCGACCCC
CACCCCTACGCCGACAGACCCTGAGCATAGCGGTAGTTGCATGGCAGTCTACAACGTGGTCAGTTCATGGGCCGGGGGATTCCAGGCAAGCGTGGAAGTCATGAACC
ACGGCACGGAGCCGCGCAACGGGTGGGCGGTTCAATGGAAGCCGGGGAGCGGTACCCAGATTAACAGTGTATGGAACGGATCGCTGTCCACCGGTAGCGAGGGACG
GTCACAGTGCGGGACGTCGACCACAACCGTGTAATCGCACCGGATGGTAGTGTGACGTTCGGTTTCACCGCCACATCAACCGGCAATGACTATCCCGCAGGGACGAT
CGGATGCGTGACCTCGTAG

>ActE GH48 (SEQ ID NO:19)

ATGGCAGCACTTGCACTCCGCTGGGGATGACGGCCGCAGCGGGTACGGAGGCACAGGCCGCAGCGGTAGCCTGTAGCGTCGATTACACCACCAGCGACTGGGGCAG
TGGTTTCACTACAGAGCTCACATTGACCAACCGCGGAAGCGCAGCCATCGATGGCTGGACGCTTACATACGACTATGCGGGTAATCAGCAGCTGACGAGCGGATGGA
GTGGTACCTGGTCCCAGAGCGGCAAAACAGTCTCTGTCAAAAACGCAGCCTGGAATGGAGCAATTGCGGCGGGAGCAGCGGTAACGACAGGTGCCCAATTCACGTAC
AGTGGAGCCAATACCGCCCGACAACCTTCGCAGTAAACGGAACCGTGTGCGCCGGAGCACATCAGCCGCCAATCGCAGTCCTGACCAGTCCGGCAGCCGGAGCAGT

FIG. 14

Example 2 DNA sequences

TTTCTCGGCGGGGGATCCAGTGCCCTTGGCGGCGACAGCGGCAGCCGCAGACGGTGCAACAATCTCGAAGGTCGAATTTTACGACGACACGACGCTGCTCGGTACCG
ACACAACATCGCCGTACAGTTATGAGGCCGGACAGCTCGCCGCAGGTTCTCACAGTGTATACGCAAGAGCCTACGACTCTCTGGGAGCCTCAGCAGATAGTCCTCCG
GCGGGCATAACGGTCGTCACAGGACCGGCGGTCGTAGTATCACCAGCGCAGCTGGGTGTGCAGCAAGGTAGGAGCGGAACGTTCGACGTATCCCTGAGCACGGCCCC
CGCAGCTGACGTGACCGTGACAGCCGCACGTTCGGCAGGTAATACGGGCTTGTCGGTGACCGGGGGCAGCACGCTTACCTTCACACCCGCCAACTGGTCGACGCCGC
AAAAAGTGACAGTCACAGCAGACGGATCGGGAACGGGTGCGGCAACATTCACGGTCACTGCACCGGGTCACGGCAAGGCAGAGGTGACCGTCACGCAGCTGGCGGCA
GCGAAGGAGTACGACGCCCGCTTCCTTGACCTCTACGGAAAAATCACGGACCCCGCGAACGGGTATTTCAGCCCGGAGGGTATTCCCTATCACTCGGTGGAAACCTT
GATCGTTGAAGCCCCGGACCACGGACATGAAACCACGTCGGAAGCATATTCCTACCTGATATGGCTGCAGGCAATGTATGGGAAAATCACAGGAGACTGGACGAAGT
TCAACGGAGCATGGGATACCATGGAAACGTACATGATCCCGACCCACGCAGACCAACCGACTAATAGCTTCTATGATGCGAGTAAGCCCGCAACATACGCCCCGGAG
CACGACACCCCCAATGAATATCCGGCAGTCCTGGACGGTTCGGCAAGTTCCGGAAGCGACCCCATAGCCGCAGAGCTCAAATCGGCATATGGTACGGATGACATCTA
CGGCATGCACTGGATCCAGGATGTGGACAATGTCTATGGTTACGGAAACGCCCCGGGCACCTGTGCAGCGGGGCCCACACAGGCAGGTCCAAGCTACATCAACACGT
TCCAACGGGGGTCCCAGGAGAGCGTATGGGAGACGGTCACCCACCCGACATGCGACAATTTCACGTATGGAGGCGCAAACGGTTACCTCGATCTGTTCACCGGCGAT
TCGTCGTACGCGAAGCAGTGGAAGTTCACAAATGCCCCGGACGCAGACGCCCGCGCCGTGCAAGCAGCATATTGGGCGGACGTGTGGGCCAAGGAACAAGGCAAGGC
AGGAGAGGTCGCAGACACAGTGGGAAAGGCAGCGAAGATGGGTGACTATCTGCGCTACAGCATGTTCGACAAGTATTTCAAGAAGATTGGCGATTGCGTAGGACCGA
CCACATGCCCCGCAGGTTCGGGCAAGGACTCCGCACACTATCTTATGAGCTGGTACTATGCATGGGGCGGCGCCACGGACACTTCGGCAGGCTGGTCCTGGCGCATC
GGTTCCAGCCATGCACATGGTGGCTATCAGAACCCGATGGCAGCGTACGCACTGTCCTCCGTAGCAGATCTCAAGCCGAAGAGCGCCACGGGTGCACAAGATTGGGC
AAAGAGTCTGGACCGGCAGTTGGACTTCTACCAGTGGCTGCAGTCCGACGAGGGCGCGATCGCGGGGGGTGCAACCAATAGCTGGAAGGGATCGTATGCACAACCGC
CCGCGGGCACGCCCACCTTCTATGGAATGTACTATGACGAAAAGCCGGTGTATCACGACCCGCCGAGCAACCAATGGTTCGGGTTCCAGGCATGGAGCATGGAGCGA
GTCGCAGAATACTACCATGAGTCGGGCGACGCACAGGCAAAGGCAGTCCTGGATAAGTGGGTGGACTGGGCCCTCTCAGAAACGACAGTCAACCCCGACGGAACGTA
TCTCATGCCCAGCACATTGCAGTGGTCGGGTGCGCCGGATACATGGAATGCAAGTAACCCGGGTGCAAACGCCCAACTCCACGTGACCGTGGCAGACTATACAGACG
ATGTCGGCGTGGCCGGGGCATACGCCCGCACGCTTACGTATTATGCCGCAAAAAGCGGCGACACGGAAGCAGAGGCGACCGCCGAGGCACTGCTGGATGGTATGTGG
CAACATCACCAGGACGACGCGGGTGTGGCAGTCCCCGAAACCCGCGCGGACTATAATCGATTTGACGATCCGGTGTATGTCCCGGGAGGTTGGACTGGCGCCATGCC
GAACGGAGACACAGTGGATGAGGACAGTACGTTCTTGTCAATCCGTTCGTTTTATAAAGACGATCCCAACTGGCCGCAGGTCCAGGCATATCTGGACGGTGGTGCCG
CACCGGTCTTCACTTACCATAGATTCTGGGCACAAGCAGATATTGCACTGGCCCTGGGTGCATACGCAGACCTCCTCGAATGA

>ActE GH5 (SEQ ID NO:20)

ATGAAGCGCTTCCTGGCACTCCTCGCCACCTGTGCAACGGTCCTCGGGCTGACCGCCCTTACAGGACCCCAAGCAGTAGCCGCGGCGGGATGCACCGCCGATTATAC
CATAACGTCGCAGTGGCAGGGCGGATTCCAAGCAGCAGTAAAAGTGACCAATCTGGGTACACCGGTCACCGGTTGGAAGCTCACATTCACATTGCCGGATGCAGGGC
AGAAAGTGGTGCAGGGCTGGAACGCAGCGTGGAGCCAATCGGGATCGGCGGTGACAGCCGCAGGGGCCGACTGGAATGGTACCCTTGCAACCGGTGCGAGTGCAGAG
GCGGGCTTCGTCGGTTCGTTCACAGGGGCCAACCCGCCACCGACAGCGTTCGCACTCAATGGAGTCGCCTGTACCGGTTCAACCGGTGAGCCACCGGCGGGAAGCGA
TGGCGGCACACCGGTCGATGTAAACGGTCAGCTCCATGTATGTGGAGTCAACCTGTGTAACCAGTACGACCGTCCAGTGCAATTGCGCGGTATGTCCACCCACGGTA
TCCAGTGGTTCGACGCATGCTATGACGCGGCAAGTCTGGACGCGCTGGCCAACGACTGGAAGTCCGACCTCCTGCGAATTGCAATGTATGTGCAGGAAGACGGATAC
GAGACAGACCCGGCCGGATTCACGCGTCGGGTCAATGACCTGGTAGACATGGCAGAAGCCCGCGGCATGTATGCCCTGATAGATTTCCACACGCTGACTCCCGGTGA
CCCGAATGTCAACCTTGATCGTGCCAAGACCTTCTTCGCGAGCGTGGCCGCAAGAAATGCCGGTAAAAAGAACGTCATCTATGAGATCGCAAACGAGCCGAACGGAG
TAACCTGGACAGCAGTCAAGTCGTATGCCGAGCAGGTGATACCCGTCATCCGCGCAGCAGACCCGGACGCAGTGGTAATCGTGGGAACCAGGGGTTGGAGCAGTCTC
GGTGTCAGCGACGGATCGGACGAGAGTGAAGTGGTCAACAGTCCGGTGAATGCCACCAACATTATGTACGCATTCCACTTTTATGCCGCGAGCCACAAAGACGCGTA
CAGAAGTACGCTCAGCAGGGCGGCAGCACGTCTTCCCCTGTTCGTCACAGAATTCGGTACCGTAAGTGCCACCGGTGGAGGAGCCATGGATCGGGCAAGCACCACCG
CGTGGCTGGACCTGCTCGATCAGCTCAAAATCTCGTATGCAAACTGGACATACAGTGACGCACCGGAGAGCTCCGCGGCCTTCCGCCCGGGGACCTGTGGTGGAGGT

FIG. 14 (continued)

Example 2 DNA sequences

GACTATTCCGGATCAGGTGTATTGACGGAGAGCGGCGCACTTCTCAAGAATCGTATAAGTACACCGGATTCATTCCCGACTGGTTAA

>ActE GH9 (SEQ ID NO:21)

ATGTGGTGCCACCCCTACCTGCGTCTCCGCACCAGCGGACGAAAGGTATCCAGTGTAAATGCTTTGCCTCCCCCAGCACGTCCTGCACCTGTGCGGCCACGGTCCCG
GTACGGTCGCCGGGTCCTCGGAATGTCGGCGGCCGCACTCCTGTGTGCCGGAGCACTCGCAGTACCGGGTACAGCGATGGCAGATGATGCCGAACCGGGGCCGGGTC
CAGAGCAGATCACGAACGGTGACTTCGCCACCGGAACGTCGGCACCGTGGTGGTGGACGCCCAACGCGTCCGCAGCCGTGTCGGAAGGTCGTCTGTGCGTAGAGGTG
CCGGCAGGCACGGCCAATGCATGGGATGTAATAGTCGGCCAGAACGACGTACCCATCGTCGCGGGTGAAAGTTACGAGCTCAGTTACACCGCCCGCTCGACAGTCCC
GCTCACGGTGCAAACCCGGGTCCAAGAGGCAGTGGAGCCGTACACCACGGTACTGGCCACCGCAGACCCCGTAGGTGCGGAGGATACACGCGTGGCACGCACGTTCA
CGGCGTCCGTCGACCAACCGGCGGCATCAGTACAGCTGCAGATAGGCGGAGGAGAACGGGCAACCACCTTCTGTTTGGACGACGTGTCTCTGCGCGGAGGCGCAGAG
CCCCCGGTGTATGTCCCGGATACAGGGAGTCCGGTGCGCGTGAACCAGGTAGGTTACCTTCCCAGGGGACCAAAGTCGGGCACAGTGGTCACCGACGCAGAAGCGCC
CCTGACGTGGACCGTGAAGGCAGAGGACGGTTCGACCGCGGCCACCGGTACGACCGTCCCGCGGGGAGAAGACCCGAGCTCGCGCCGACGTGTGCACACATTCGATT
TCGGTGACCTCACCACAGCCGGCGACGGATATACCGTAGAGGTCGACGGTGAGGTAAGCGAGCCCTTCTCAATTCGCGGTGATCTGTACGACTCGCTGCGTAGCGAC
GCCCTCGCGTATTTCTATCATAACCGATCGGGAATCGAGATCGACGCCGACCTGGTCGGGGAGCAATACGCACGTCCCGCAGGTCACATTGGCGTCGCACCGAATAA
GGGAGACACCGACGTCCCGTGTCGCCCTGGAGTGTGTGATTACCGCCTCGACGTCTCCGGGGGATGGTACGACGCGGGCGATCACGGGAAATATGTAGTGAACGGAG
GTATCAGCGTGGCCCAGCTTATGGCAACGTACGAACGTACCCTCACGGCGCCGGATGCGGAGTCGGCCGAACTCGGAGATGGTGCACTCCGCGTCCCGGAGCGCGAC
AATGGAGTGCCTGACATTTTGGACGAAGCACGGTGGGAGATGGATTTCCTGATCAAGATGCAGGTACCGGCTGGCGAACAACTCGCAGGCATGGTGCACCACAAAAT
GCACGACGCCGAATGGACCGGACTCCCAATGAAGCCCCATCTCGACCCCCAGCAGCGCGAGCTGCATCCTCCGTCCACGGCAGCAACACTCAATTTGGCAGCCACCG
CAGCACAGTGTGCACGTCTGTATGCCCCATTCGACGCAGACTTCGCCGATCGCTGTCTGAGGGCCGCAGAAACCGCCTGGGACGCAGCCAAAAGGCACCCGGACGTC
CTCGCAGATCCCAACGACGGAATCGGTGGCGGTGCATATAATGACGACGATGTATCAGACGAGTTCTACTGGGCAGCGGCCGAGTTGTTCACCACGACAGGGAAGGA
TATTTACCGTCAGGCGGTCTTGTCGAGCGCCTGGCATGGAGACGCAGGTGCCGTATTCCCGGCGGGCGGAGGTATCTCGTGGGGTAGCACGGCAGGCCTCGGTGTCC
TTACCCTGGCAACAGTCCCCAACGCTTTGACCTCGGATCAGCTCGCACAGGTGCGAACCGTAGTGACCGAGGGAGCCGACCGCTATGCAGCCCAGTCAAGGGAACAA
GCATACGGGCTCCCGTATGCGCCCCGTGGCGAGGACTATGTATGGGGCAGCAATTCGCAGGTCCTGAATAACATGGTGGTCTTGGCCACGGCACACGACCTGACAGG
TGACGCAGCGTACCAGGATGCAGTGCTCCGGGGCGCCGACTATCTCCTGGGCAGGAATCCTCTTAACCAAAGCTACGTAACCGGGTATGGTGAACGTGACAGCCACA
ATCAGCACCATCGTTTTTGGGCGCACCAAAACGATCCGTCGTTGCCCAACCCGGCCCCCGGCTCGATTGCCGGCGGACCCAACCTCACAGCAATCGCAAGTGGCGAT
CCCGTAGCAGCGGAGAAGCTGAGCGGTTGTGCACCCGCAATGTGCTACGTGGACGATATTGGAAGTTGGGCAACCAACGAAATCACGATCAACTGGAACGCGCCCTT
GGCCTTCATCGCCTCCTATCTGGACGACGCAGGTGAGGGAGGGCAGACAGCCGCAGCCCGCACGTGCCAAGTCACCTATTCGAGCCACCCGTGGAACAGTGGATCAA
CAGTAACGGTCCGTGTGGAGAATACCGGTTCGGATCCGGTGTCGCCCTGGGCCCTCACGTGGTTGCTGCCGGGGGAACAGCGCCTCAGTCACACTTGGTCAGCCGAG
TTCGACCAACATGGCCGTACGGTCAGCGCACGCCCCCTGTCGTGGAATCGTACACTGGCACCGGGAGCGGCAGTGGACTTCGGATTCAACACGTCAGCCGCAGGCTC
GAGTCCGGAGCCGGGGGCATTCAAGCTCAACGGAAGGGCATGTAGCGCAGGTTGA

>B6 GH6 (SEQ ID NO:22)

ATGAGTCGTACGAGCCGAACCACGCTGCGCCGGTCGCGCACAGCCCTGATCGCAGCAGGAGCCCTCGTAGCAGCAGCAGCGGGCAGTGCAGCCGCAGCCGCACCTTT
CGCAGCGTCCGCAGCAGCCGCAACCGGATGCACCGTAGACTATAAAATCGAGAACCAGTGGAACGGAGGACTGACAGCCGCAGTCAACGTCACCAACAACGGCGCGC
CGGTAACGTCATGGCAGCTGCAGTGGACCTTCAATGGGGGAGAACAAGTCTCCCAGGGATGGAACGCAACAATCAGCCAGAGCGGGTCAGCAGTAACTGCAAAAGAT
GCCGGTTACAATGGTACACTGGCAACAGGCGCCAGCGCATCGTTTGGATTCAACGCCACAGGTAATGGCAACAGTACCGTCCCGGCGACATTCAAACTGAACGGAGT
GACCTGTAACGGGGATACCACCGGACCCACAGACCCAACGGATCCTACGGACCCGACGGATCCCCCGGCAGGGAATCGCGTGGACAACCCGTATCAGGGCGCAAAGG
TATACGTGAATCCGGAGTGGAGCGCGAACGCCGCAGCGGAACCTGGGGGTTCCCGTGTCGCAAACCAACCCACCGGAGTGTGGCTCGACCGCATAGCAGCGATCGAG

FIG. 14 (continued)

Example 2 DNA sequences

GGTGCCAATGGATCGATGGGTTTGCGTGAGCATCTGGACGAAGCCTTGACCCAGAAGGGTAGCGGAGAGCTGGTCGTACAACTCGTGATTTATGACTTGCCGGGTCG
CGACTGTGCGGCCCTGGCATCCAACGGCGAACTCGGACCGACAGAAATCGGCAGATATAAGACCGAGTACATCGACCCAATCGCGGCCATAGTCGCGGACCCCAAAT
ATGCCGGACTGCGTATCGTAACAACGGTGGAAATAGACAGCCTGCCTAATCTGGTAACGAACGCAGGTGGCCGTGAAACCGCAACACCGGCATGTGATGTCATGAAG
GCAAACGGAAACTATGTCAAGGGCGTGGGATATGCACTGAACAAGCTCGGAGACGCGCCCAATGTCTACAACTATATTGACGCCGGTCACCACGGATGGATCGGGTG
GGACGATAATTTCGGCGCATCGGCGCAAATATTCCACGAAGCAGCAACTGCGGAGGGAGCAACCGTAAACGACGTGCACGGTTTCATCACGAACACGGCGAATTACA
GCGCACTGAAAGAACAGAACTTCAGCATCAACGATAGCGTCAATGGCACTTCCGTGAGGGAATCGAAGTGGGTCGACTGGAACCGCTACACGGACGAGCTCAGCTTC
GCACAAGCGTTCCGGAACGAACTTGTGAGCGTCGGCTTCAATTCGGGTATTGGGATGCTGATCGACACCAGTCGAAACGGCTGGGGAGGTAGCGCACGGCCCAGTGG
ACCAGGGGCTACCACCAGTGTCGACACGTATGTGGATGGTGGCCGCTATGACCGGCGCATCCACCTGGGAAACTGGTGCAATCAAGCCGGAGCAGGTTTGGGGGAAC
GACCAACCGCAGCCCCCGAGCCCGGTATCGACGCATATGTTTGGATGAAGCCGCCGGGAGAGTCGGACGGGTCCAGCTCCGAGATCCCTAATGATGAGGGTAAAGGC
TTCGACCGCATGTGTGACCCGACATACACGGGAAACCCCCGGAACAACAACAATCCGTCGGGCGCATTGGGGGGAGCGCCCGTGAGTGGTAAGTGGTTCTCGGCCCA
GTTCCAGGAGCTCATGAAGAACGCATATCCTGCACTCTGA

>B6 LPMO (SEQ ID NO:23)

ATGGCCGGCAGGTCCCGCCTGATTTCCCTCGCGGCGGTCCTGGCCACATTGCTGGGTGCACTGGGCCTCACCGCCCTCTGGCAGGGTAAGGCGGAAGCACATGGGGT
CGCAATGATGCCCGGAAGCCGGACATATCTGTGCCAAGTGGACGCCCTCTCTGGCACCGGAGCACTGAACCCGACAAACCCGGCATGTCGCGATGCGCTGAGCAAAT
CGGGTGCAAATGCCCTGTACAATTGGTTCGCAGTCCTGGACAGTAACGCCGGCGGAAGAGGTGCAGGCTACGTGCCGGATGGGACCCTGTGCTCCGCCGGCGACAGA
AGCCCGTACGACTTCAGCGCATATAATGCGGCACGTGCCGACTGGCCGAAGACGCACCTGACGAGTGGCGCAGGAATCCAGTTGCAGTATAGCAATTGGGCCGCACA
TCCGGGCGACTTCCGAGTCTACGTCACTAAGCCGTCGTGGTCACCCACAAGCGCGCTCGGATGGAACGACCTGCAGCTGGTACAGACCGTGTCGAATCCGCCGCAGC
AGGGCAGCCCTGGAGCCAACGGTGGTCACTATTATTGGGACCTCACCCTGCCGTCGGGTCGGTCGGGGGACGCACTGATGTTCATCCAGTGGGTCCGTAGCGACAGT
CAGGAGAACTTCTTCTCCTGTTCGGACATAGTATTCGACGGAGGCAAGGGCGAAGTGACCGGTATCGGGGGGTCCGGTAATGGAACACCGACACCCACACCCACCCC
CACGCCCACAGATCCCGAGCACAGCGGGTCGTGTATGGCCGTATATAACGTGGAGTCCTCGTGGAATGGAGGCTTCCAGGCCAGCGTAGAGGTAATGAATCACGGTA
CCGAGCCGCGAAACGGATGGGCGGTCCAGTGGAAGCCGGGAACGGGTACGCAGATCAACAGTGTATGGAACGGTACCCTGTCCACAGGGTCGGACGGTACCGTCACA
GTCAGGAACGTGGACCATAACCGCGTAATAGCACCGGATGGAAGCGTCACTTTCGGCTTCACCGCCAATTCGACAGGAAACGACTTCCCCGCGGGCACGATCGGATG
TGTAACGAGTTGA

>B6 GH48 (SEQ ID NO:24)

ATGGCAGCACTGGCCTTGCCGCTGGGTATGACCGCAGCGGCAGGCACCCCGGCACAGGCAGCAGCGGTAGCATGCTCAGTAGACTACAAGGCCAACGATTGGGGTTC
GGGCTTCACCACCGAACTGACACTCACAAATCGCGGTAGTGGTGCGATCGACGGATGGACACTCACGTACGATTATGCCGGTAACCAGCAGTTGACATCAGGATGGT
CGGGTGTGTGGAGTCAGAGTGGTAAGACGGTAACAGTGAAGAACGCAGACTGGAACGGAACCGTCGCGGCCGGCCAGGCAGTCACAGCCGGTGCACAGTTCACGTAT
AGTGGAACCAATACAGACCCGACAGCGTTCGCAGTGAACGGGACCGTATGCGCGGGAGCACACCAGCCCCCGATAGCCGTCCTCACCAGCCCTGCAGCAGGAGCGGT
CTTCACAGCAGGCGATCCGGTACCGCTGGCCGCAACCGCAGCAGCAGCGGACGGTGCGACCATTTCCAAGGTGGAGTTCTACGACAACACTACACTGCTCGGCACAG
ACACTACCTCACCATACTCATATACAGCGCAAGGACTGTCAGCCGGGAGTCATTCCGTGTATGCACGCGCATACGACTCATTGGGTGCGAGCGCAGAAAGTCCGCCA
GCCGGAATCACCGTCGCAGCGGGTCCGGCAGTAGTCGCAACACCCGCCCAGCTCGGAGTACAGCAGGGAAAGTCGGGCACCTTCAACGTGTCCCTTTCAACTGCACC
GGCCTCAAATGTCACAGCAACCGTCGCACGGACGGCAGGAAATACAGGATTGAGCGTCACCGGAGGCGCGTCACTGACCTTCACGCCCGCCAACTGGTCGACCCCTC
AAAAAGTAACCGTCTCCGCAGATGGTTCGGGAACAGGAGCAGCAACGTTCACAGTGAGTGCGCCTGGTCACGGAAAGGCAGAGGTAACGGTAACGCAGCTCGCGGGT
GCAAAGGAGTATGATGCACGATTCCTGGACTTGTACGGCAAAGTGACCGATCCGGCCAACGGGTACTTCTCTCCGGAGGGAATACCATACCACTCAGTGGAGACGCT
GATTGTCGAAGCGCCGGACCACGGTCATGAGACGACCAGTGAAGCCTATAGCTACTTGATATGGCTGCAAGCAATGTACGGCAAGATCACGGGTGACTGGACCCGCT

FIG. 14 (continued)

Example 2 DNA sequences

TCAACGGCGCGTGGGACACAATGGAAACCTATATGATCCCCACACACGCAGACCAGCCGACCAATGCATATTACGACGCCAGTAAGCCTGCAACATACGCACCCGAG
CACGACACCCCAAACGAATACCCGGCGGTACTTGACGGAAGCGTATCATCGGGCTCAGACCCCATCGCCGCCGAGCTGAAGTCGGCATATGGAACCGATGACATCTA
TGGAATGCACTGGATCCAGGATGTCGACAACGTATACGGCTACGGGAACAGTCCGGGAACGTGTGCTGCAGGGCCAACCCAGACCGGACCGAGCTATATCAACACCT
TCCAGAGGGGTCCCCAGGAGTCGGTGTGGGAGACGGTCACGCACCCAACATGCGACAATTTCACCTACGGGGGAGCAAATGGATATCTCGATCTGTTCACAGGTGAC
TCAAGCTATGCGAAGCAATGGAAGTTCACGAACGCCCCCGACGCGGACGCAAGAGCAGTACAAGCAGCATACTGGGCAGACGTATGGGCCAAAGAACAAGGTAAGAG
TGCAGACGTGGCGGGCACAGTGGGTAAGGCGGCAAAGATGGGAGACTATCTGCGGTACTCAATGTTCGACAAGTATTTCAAGAAGATCGGTGACTGCGTCGGCCCGA
CCACCTGCCCGGCAGGCTCTGGTAAAGATAGTTCTCACTACCTCATGAGTTGGTACTATGCCTGGGGCGGAGCAACCGACACCTCGGCAGGGTGGGCATGGCGTATA
GGAAGTTCACACGCACACGGCGGTTACCAAAACCCTATGGCAGCGTATGCGTTGTCGTCGGTGGCAGACCTGAAGCCAAAGAGTGCAACGGGCCAGCAGGATTGGGC
AAAGAGCCTGGACCGCCAGTTGGACTTCTACCAATGGTTGCAGTCGGACGAAGGGGCGATCGCAGGAGGCGCCACCAACTCGTGGAAGGGTGGGTATGCCCAGCCGC
CGGCGGGTACACCCACGTTCCACGGAATGTACTACGACGAGAAGCCCGTATACCACGACCCGCCCTCCAATCAGTGGTTCGGATTCCAAGCCTGGTCAATGGAACGG
GTCGCAGAGTATTATCATGAGTCAGGTGATGCACAGGCGAAGGCCGTGCTCGACAAGTGGGTCGATTGGGCACTGTCGGAAACTACAGTCAATCCCGACGGAACCTA
CCTGATGCCATCAACACTGCAGTGGAGCGGCGCCCCTGACACCTGGAACGCATCAAACCCGGGATCGAATGCGGGTCTGCACGTGACAGTAGCAGACTATACGAACG
ACGTGGGTGTGGCCGGTGCATACGCGAGGACGCTGACATATTACGCCGCAAAGAGCGGAGACGCCGATGCCAAGGCAACCGCAGAGGCACTGCTCGACGGCATGTGG
CAGCACTACCAAGATGACGCGGGAGTGGCCGTCCCCGAGACGCGCGCAGATTATAACCGGTTCGACGATCCAGTGTACGTCCCCGGTGGCTGGACCGGTGCCATGCC
GAATGGGGATACCGTGGACCAGGACTCGACATTCGTATCCATAAGGTCCTTCTATCAGGATGACCCCAACTGGCCGAAGGTCCAGGCCTACCTTGACGGTGGAGCGG
CGCCGGTCTTCACGTACCACCGTTTTTGGGCCCAGGCAGATATCGCTTTGGCCTTGGGTGCCTATGCAGACCTGCTCGAATGA

>B6 GH12 (SEQ ID NO:25)

ATGAAGAGCCTCATCGCCTCCCTCAGGTCAGCAGGCACGGCAGTCACAGCAAGCCTGGTGGCGCTCGCCACCTGCGCAGCCTTGGGAGCACTGGCAGCACCGGCACA
GGCAGCAGATTCGATCTGTGGCCAGTATGGAACGACGGTAATCCAAGACCGCTATGTCGTCCAAAACAACCGATGGGGAACCACGGACGCGCAGTGTGTGGACGTGA
CCGACGATGGGTTCACCGTAACGCGCGCAGACGGCTCGGTCCCCACCAATGGAGCACCGAAGTCGTATCCGAGCGTCTATAACGGTTGTCATTACACAAATTGTTCG
CCGGGAACCGAGCTCCCGAAGCGGCTGGATAGTATCAGCTCCGCCCCCACAGCGATCACATATACGTACGTCGACGGTGCCGTATACGACGCAGCATATGACATCTG
GCTCGATCCTCAGCCGAAAAAGGACGGCGTGAACAGGACAGAGATCATGATCTGGTTCAATCGGGTGGGGCCCATACAGCCGGTCGGTAGCCAGACGGGTACCGCCA
CGGTGGCAGGTAGAGGGTGGGAAGTCTGGACCGGTAACAACGGAGGTAATGACGTCATTTCCTTCGTATCCCCGTCGGCAATCTCCAGCTGGAGTTTCGACGTCATG
GACTTCGTAGACGCAACGGTGGCGCGCGGAATGGCACAGAACTCATGGTATCTGACCTCGGTGCAGGCGGGCTTCGAACCGTGGCAGAACGGAGCCGGCCTCGCAGT
ATCGTCCTTCTCAAGTTCGGTGTTGACCGGTGGCGGTTCAGAGGGACCCGGCGAGCCGGGAACACCGGCCGATGGTCCGTGCGCAGTCAGCTATACCGCCAACGCAT
GGACAGACGGATTCACGGCAGACGTGAAGGTCACCAATACAGGCACAGTGCCAGTCTCGGGATGGCGGTTGGGTTTCACACTGCCCCAGGGGCAGACGGTCACCCAG
GCATGGAACGCCACGGTAACCCCGTCGAGTGGAGCAGTGACGGCCACCGGTGCAGCGTTCAACGCAGAGATAGCAGCAGGGGCAAGTCAGAGTTTCGGATTTCAAGG
TACCCACTCGGGAACCTTCACAAAGCCCGACCGTTTCACCCTCAACGGTGCGGTCTGTACAGTCGGCTGA

>B6 GH9 (SEQ ID NO:26)

ATGAACGCATTGCCTCCACCGGCGCGGCCTGCCCCAGTACGTTCCCGCTCGCGTTATGGACGACGTGCACTGGGAATCAGTGCAGCGGCGTTGCTCTGTGCAGGCGC
GCTCGCGGTCCCCGGCACAGCACTGGCGGATGATGCAGCCCCTGGTCCCGAACAGATCACCAACGGAGACTTCAGCGCCGGTACAGCGCCATGGTGGTGGACGCCGA
ACGCCTCCGCGGCAGTGAGCGAAGGCCGATTGTGTGTAGAGGTCCCCGCCGGAACCGCAGAAGCCTGGGACGTAATCGTGGGTCAAAACGATATCCCTATAGTCGCA
GGCGAGTCCTACGAGCTGAGTTATACAGCGCGCAGTACGGTACCGCTCACCGTGCAGACGCGCGTCCAGGAAGCAGTAGAGCCATACGGAACTGTGCTCGCCACCGC
AGATCCGGTCGGAACGGAGGATACCCAGGTGACACGTACCTTCACAGCATCCGTCGATCAACCGGCGGCCAGCGTCCAGCTCCAAATTGGGGGGGGAGAACGCGCGA

FIG. 14 (continued)

Example 2 DNA sequences

CGACCTTCTGCCTTGACGACGTCAGCCTCCGTGGCGGAGCAGAGCCTCCCGTATATGTGCCGGACACGGGATCCCCAGTCCGAGTCAACCAAGTGGGATATCTGCCG
CGCGGTGTCAAGAGCGGCACAGTCGTAACAGACGCACCGCTCACCTGGACAGTGAAGGCCGGGGATGGAAGCACCGCAGCAACTGGAACCACAGTGCCGCG
GGGTGAGGACCCCCAGTTCCCGACACGACGGGTCCACACATTCGATTTCGGTGGACTGACCACGCCGGGCGATGGTTACACAGTAGAGGTGGACGGAGAGGTATCGGAGC
CCTTCTCGATCCGAGGTGACCTCTATATGATGGGTTGCGCTCCGATGCCTGGCCTACTTCTATCACAACCGGAGCGGTATCGAAATAGATGCAGACCTGGTGGGCGAG
GAATATGCCCGTCCCGCAGGGCACATTGGCGTCGCGCCGAACAAGGGAGACACGGACGTCCCGTGTAAGCCAGGAGTCTGTGACTATCGGCTCGATGTCTCACGGCGG
TTGGTACGACGCCGGCGACCACGGTAAGTACGTAGTCAACGGGGGAATCAGCGTGGCACAGCTTATGTCCACATATGAGCGCACTCTCACCGCGGACAACGCAGAAT
CGGCACAGCTGGACGATGGCGCCCTGAGGGTCCCGGAACGTGGAAATGGAGTGCCGGACATCCTGGATGAGGCACGATGGTTCCTGATAAAGATGCAG
GTCCCTGCCGGGGAGCCGTTGGCAGGAATGGTGCATCACAAAATGCACGACGCCGAGTGGACCGGACTGCCGATGAAGCCGCACTTGGACCCGCAACAGCGTGAACT
TCATGCACCCTCCACCGCAGCCACCCTCAACCTGGCGGCGACGGCAGCACACAGTGCGCCCGACTCTATGCGCCCTATGACGAGGACTTCGCCGACCGTTGTCTCCGAG
CAGCAGAAACCGCATGGGACGCAGCGAAAAGGCACCCGGATGTCTTCGCCGACCCCAATGACGGTGTCGGTGGTGGTACATACGATGATAATGACGTATCCGACGAG
TTCTATTGGGCCGCGGCCGAACTCTTCACCACCACAGGCAAGGACACCTATCGTCAAGAGGTGTTGTCGAGTGATCTTCACGGTGATGCAGATGCCGTCTTCCCCGC
AGGAGGCGGCCTCAGCTGGGGTGCCACAGCAGGGCTCACACTGGCCACGGTACCGAACAACCTGACCACGGACCAGCTCGATGGTGTGCTGGGCAACCG
TCACCACCGCAGCAGATCGGTATGCGGCGCAATCCCGCGCCCAGGCATATGGCCTCCCGTACGCACCGCGCGGAACGGATTACGTATGGGGTAGCAACTCCCAGGTA
CTCAATAACATGGTGGTCCTCGCCGTAGCACACGACCTGACCGGAGAAGCGGCATATCAGGACGCGGTACTCCGGGGTGCAGACTACTTGTTCGGGCGCAATCCGCT
GAATCAGTCGTATGTCACGGGATACGGCGAGCAGACTCTCACAACCAGCACCACAGGTTCTGGGCACATCAATATGATAGCAGTTTGCCTAATCCCGCACCAGGTT
CCGTAGCAGGTGGCCCGAACCTCACGGCAGCAGGAAGTGGTGACCCCGTCGCGGCCGAAAAGCTGTCGGGCTGCGCCCCGGCAATGTGCTACATCGACGACATCGGG
AGTTGGAGCACCAACGAGATTACAGTAAATTGGAACGCGCCGCTCGCATTCATTGCCTCGTACCTTGACGACGCCGGAGATGGTGGCCAGACCACAGCGTCACGTAC
ATGCGAAGTCACGTATAGCTCGCACCCGTGGAGCGGGGGAAGTACCGTCTCGGTGCGAGTAGAGAATACAGGTTCGGCCCCAGTGGAACCCTGGTCACTGACGTGGT
TGCTGCCGGGCGAGCAGAAGCTCTCCCACACCTGGTCAGCCGAATTCGAGCAACACGGGCGCACCGTGTCAGCAAGGCCGCTGGCGTGGAACCGGACCCTTGCACCG
GGAGCCGCAGTAGACTTCGGCTTCAATACGAGCGCGACAGGAGCAGCGGCCGATCCAGGCACGTTCAAGTTGAACGGTCGCGCCTGTGCATCGGGCTGA

>95 GH6 (SEQ ID NO:27)

ATGTCAACCCGTGGGAACCATAAAACAGGGTCTGCGCCGTAGACTCGCAGCAGCAAGTGCACTGGCAATGGGAGCGGCACTCGCAGTAGCAATCCCGACACAACCGCAGA
CGCCGCAGCCGCCCGAGTCGATAATCCATATGTCGGTGCAAAGGCATACGTGAACCCAGACTGGAGTGCAAAAGCAGCGGCCGGAACCGGGCGGAGCAGCGATTGCCG
ATACACCGGCGTTCGTGTGTGGATGGACCGCATCGCAGCAATCGGTGGTACACCGGGTGCCATGTCGCTCAGGGAACACCTGGACACGGCACTGGATCAGGGTGCAAAT
CTCTTCCAAGTCGTCATCTACGACCTCCCGGGTCGTGACTGCGCAGCCCTTGCAAGTAATGGGGAGCTGGGACCGAGCTCGATAGGTATATAAGTCCGAATACAT
CGACCCGATCAGTGAGATCCTCGCGGACCCGGCATACGCGAATCTGCGGATAGTCACAATCATCGAGCCCGACTCGCTGCCCGAATATTGTGACGAATGCGGGTGGCA
CCGCAGGATCGACAGACGCGTGTGCAACAATGAAGGCAACGGTAATTATGAGAAAGGCGTCGGTTATGCACTCCACACCCTCGGTGCCATCCCGAATGTATATAAC
TACGTGGACGCAGCCCACCACGGCTGGTTGGGGTGGGATAGCAAACATGGTGCCGGCCGGGGTGGAGTTCAAGAAGGCAGCAACAAGTGAGGGAGCAACCGTGGACGA
TGTCGCAGGATTCATAGTAAATACGGCGAACTACTCCGCACTTAAGGAGCCCAATTTCAAAATAACCGACTCAGTGAACGGCACTACGGTGCGTCAGAGTAAGTGGG
TCGATTGGAACTACTATACTGACGAGCTCAGTTTCGCGCAGGCCCTGCGCACCCAGCTGGTAGGCCAGGGATTCAACTCTAACATCGGTATGCTCATTGACACGGCA
CGCAATGGATGGGGAGGCTCGGATCGTCCGACATCAGCAGGGCCGCTGACGTCGGTCGACGACTACGTCAACGGTGGCCGGGTCGATCGCCGGATCCATGCGGGAAA
CTGGTGCAATCAGTCTGGCGCAGGAATCGGCGAGAGGCCGACCTCAGCGCCCGAAGCGGGAATCGACGCGTATGTATGGGCAAAGCCCCCCGGCGAGTCGGACGGGA
GTAGTCAGGCAGAAGATAACGACGAGGGAAAAGGTTTCGATCGAATGTGTGACCCGACATATGAAGGCAACGGAAGGAACGCAAGACGGCGCGCGTTGCCG
AATTCCCCAGTAGCAGGGCACTGGTTCAGTGCACAAGAGCTTGTCCGTAATGCATATCCCCCGATCGACGGTAGCGGAGAGAACCCGGGTGGCGGCGGAGA
CGACGATACCCAGGCGCCGACAGGGCTCACATCCTCGGCGAAGACCAGTTCAAGCGTCAGTCTCTCATGGACCGCCTCCTCGGACAATAAAGCAGTGA
CCGGTTACGATGTCTACCGGGGAGGAACGAAGGTAGGCAGCACGACATCGTACACGGGACTGAGCGCCTCGACGGCATATTCATACACCGTGAAG

FIG. 14 (continued)

Example 2 DNA sequences

GCGAAAGATGCCGCCGGGAACGTGTCGGCAGCATCGTCAGCACTGAGCGTCACAACGTCAGCCGGGGGAGGCACAGGAACGGGAAGCCTGAAGGTCCAATATAAAAA
TAACGACAACAGTCCGACAGACAACCAGATCAGGTTCGGTCTGCAACTCGTGAATACGGGATCCTCGGCCGTGGACCTGAGTACCGTCAAGCTCCGCTACTGGTTCA
CCCCAGAATCCGGCAGCTCCACGTTCGGGACAGCCTGCGATTATGCAGTACTGGGATGTGGTAAGCTGTCCCTTGCCGTACAATCAGGCGGAAGTGCGGCAGGAGCA
AGTCACTACCTCGAGGTCAGCTTCGGGTCGGGGAGCCTTGCGGCAGGTGCATCCACGGGGGAAATGCAGCTGCGACTGAACAAGAGCGATTGGTCGAACTTCAATGA
GGCGGACGACTATAGTCATGGGACCGGAACCTCGTTCGCCGACGCATCCAAAATAGGAGTGTATACCGCCGGCGCGTTGTCCTGGGGTACAGCCCCTTGA

>95 LPMO (SEQ ID NO:28)

ATGGCGCGCAGGCGCACACAGCTGGCAAGCCTTGCGGCCGTCCTGGCCACCCTCCTCGGTGGCATCGCCTTCACTCTGCTGGGACAGGGTTCGGCACAAGCCCACGG
CGTGACCATGTCCCCGGGATCCCGTACATACCTCTGCTGGTTGGACGCAAAGACATCGACCGGTTCACTGGATCCGACCAATCCGGCATGTAAGGCAGCACTTGCCG
AGTCCGGCGCGTCCTCGCTGTATAACTGGTTCGCCGTGCTCGACAGTAACGCAGGTGGACGAGGCGCAGGATACGTACCCGACGGCACCCTTTGTAGCGCTGGAGAC
AGGTCGCCGTACAATTTCACAGGCTATAACGCAGCCCGGGGGGATTGGCCCAGGACTCATCTGACCAGCGGCGCGAAAATCGAGGTAGACCACTCAAATTGGGCAGC
GCACCCGGGAGAGTTCCGTGTGTATATGAGCAAGCCGGGATACTCGCCGACCACGGAACTCGGTTGGGATGACCTCGACCTCATCCAGACCGTCTCTAATCCGCCCC
AAGTGGGGTCCCCGGGAACGGACGGTGGCCATTATTATTGGGATCTGACTTTGCCCTCGGGCAGGTCAGGAGATGCCGTTATGTTCATCCAATGGGTAAGGAGCGAC
AGTCAGGAGAACTTCTTCAGCTGCAGTGACATCGTCTTCGATGGCGGCAATGGTGAAGTAACCGGAATCCGCGGAAGTGGCTCGACCCCAGACCCGGACCCAACCGA
CCCGACCCCGGACCCGACAGACCCTACCGATCCGACAGACCCCCACACAGGATGCATGGCAGTGTACAATGTGACGAATAGCTGGTCAGGTGGATTCCAGGGTAGCG
TTGAAGTAATGAACCATAATACCACGGCGCTCGACGGTTGGGCGGTGCAGTGGAAACCGGGTACCGGTACGACAGTCTCCAGCGTATGGTCGGGCGTATTGTCGACG
GGAAGTGATGGTACCCTCACGGTGAAGAACGCAGACTATAATCGCAGCATCCCACCGGACGGCTCGGTCACCTTCGGTTTCACGGCGACCTCGACGGGGAACGATTT
CCCGGTGGGGTCCATAGGTTGTGTCTCCCCGTGA

>95 GH48 (SEQ ID NO:29)

ATGCTGGCAGTCGGCCTCGCACAGGGTACCGCAATCGCGAGGCCAGCAAGTGCCCAGGCAGGCACGGGTGCACGTGCGGCCGCAGCGGGAGACGATCCCTACACCCA
GGCCTTCCTGACGCAGTACGGTAAGCTGAAGGACGCTGCAAACGGCTATTTTTCACCGGATGGCTTGCCGTACCATTCGGTAGAAACCTTGATGGTGGAGGCACCTG
ATCATGGCCACCAGACGACCTCTGAAGCCGTCTCCTTCTGGATGTGGTTGGAGGCCGCATACGGTCGAGTAACGGGCGACTGGGCCCCGTTCAATGCAGCGTGGGCA
GTCGCAGAAAAGACCATTATCCCCCAGCATGCGGACCAGTCGACATCCGACTCGTATAACCCGTCCGCACCGGCCACGTATGCACCGGAGCACCCTCTGCCGAGCGG
CTACCCGTCGGCATTGGATGGTACCGTCCCGGTCGGTACAGACCCTCTCAGCGCAGAATTGGCGAGTTCGTATGGAACCATGGACGTGTATGGTATGCATTGGCTCA
TGGATCTGGACAACGTGTATGGTTACGGTAACAAGCCGGGTACGGGTGGAGAGAGCGGTCCCGGCGCAGGAGCGTCGTTCATAAATACCTATCAACGTGGTGCACAG
GAGAGCGTGTGGGAGACGGTACCGCAACCGACGACGGATCTCTTCAAGTACGGAGGGCCGAACGGATACCTGGACTTGTTCGTGGGTGACTCCAGCTACGCGAAACA
ATGGAAGTACACCAACGCACCGGACGCCGATGCACGCGCCGTCCAGGCGGCATACTGGGCATATCGGTGGGCAAGTGAGCAAGGCAAGGAATCGCAGGTGGCAGCAT
CGGTGGCGAAAGCCGCAAAAATGGGTGACTACCTCCGCTATGCCATGTTCGACAAGTATTTCAAGCGAGTCGGAGATTGTACGGACCCAAATAGCTGCCCCGCAGCG
TCGGGTCGCGACAGCCAGCACTACCTGTTGTCGTGGTACTATGCCTGGGGTGGCGCAGCGGCAGGTAGTGGAGGCGGATGGGCCTGGCGTATCGGTGACGGGGCATC
GCACCAGGGATATCAGAACCCGCTTGCAGCATGGGCCCTGAGCAACGTCCCGTCGCTGACCCCGAAGAGTGCAACGGCCCGATCGGATTGGTCCAAGTCGCTGACCC
GCCAACTCGAGTTCTTGACATGGCTGCAGTCAAGCGAGGGCGCCCTGGCAGGGGGTTGCACCAACTCATGGGAAGGCAGCTACTCAACACCCCCGGCCGGAACGCCC
ACTTTCTATGGTATGGCATACGACTGGCAGCCGGTGTATCATGACCCGGCGTCGAATAATTGGTTCGGCTTCCAAGCCTGGGGTATGGAAAGGGTGGCGGCATACTA
CTATGTAACGGGGAACGCAACAGCAGAGGCAGTGCTTTCGAAGTGGGTCGCCTGGGCATCATCGGAAACCACTATTGGATCGGACGGTAGCTTCCGTTTCCCTTCGA
CGCTGAATTGGACCGGGGAACCAGACACCTGGAACGCAGCATCCCCGGGTGATAACGCCGGACTGCATGTGTCAGTCGTAGACTATGCAAATGACGTCGGAGTCGGT
GCGGCGTATGTGAAGACACTCACCTACTACGCAGCGAAGAGCGGAGACGAAGATGCAGCCGCATTGGCAAAGGCCCTGCTCGACGCAATGGCACTCAACACAACCGA
CAAGGGAATCAGTGTCCCGGAAACGCGCCTCGACTACAATCGTTTCGATGACGAGGTCTACATCCCGTCGGGCTGGTCTGGTACAATGCCGAACGGTGACCCCGTCC

FIG. 14 (continued)

Example 2 DNA sequences

GTCGGGAAGTACTTTCATTTCCATACGGAGCTGGTATAAAGATGACCCAGACTGGCCTAAAGTACAGGCATACCTCGACGGCGGGGATGCGCCGGTATTCACCTAC
CACCGGTTCTGGGCCCAAGCCGCCCTGGCATTCGCAATTTATGCGGAACTTCTGGTAGAGGGAGGAGGTGGGGAACCTGGTGGTGACACGGAGCCGCCGAC
CGCACCGGGCGGACTCACCGTAACAGCTACAACGAAGGATAGCGTCTCCCTCAGCTGGTCGGCATCAACCGACAACACAGCAGTGACCGGGTATGACGTGTACCGTA
ATGGAGTACTGGCCGGAAACGCAACAGGCCGCACATTCACGGATAGCGGCCTCGCAGCCAATACGGAATATACATATGCGGTCGCAGCCAGGGACGCAGGTGGGAAT
ACATCTGCGCTGAGCGATGCCGTCCTGGCAAAGACAAAAACAGGTGGGAGCACGGGTACCGGCGCAGTAAAGGTCCAGTATAAGTCGACCGATAGCTCGGCAACTGA
CAACCAAATCCGTATGGGACTGCAAGTAGTCAACACCGGCTCGGCACCGGTAGATCTGTCGACAGTGAAGGTGCGCTATTGGTTCACAGCCGACGGTGGACCCTCCA
CCTTCGGAACATACTGCGACTATGCCGCATTGGGGAGCTCGACGATTACCCACACTGTCGTCGCCGTAAGCTCGCCGAAGACAGGAGCAGACCGATACCTGGAGGTC
GGGTTTACCGGTGGTGCGGGCACACTCGCAGCAGGTGCGTCCACGGGGGAGATCCAATTGCGACTGAACAAGTCGGATTGGTCAAATTTCAACGAGGCCGATGACTA
CAGCCGTGCAACCAATACAGCCTATGCAGATTCGTCTAAGGTAGGGGCCTACGTCGCAGGAGCACTCGCATGGGGAGTCGAACCCTAA

>95 GH5 (SEQ ID NO:30)
ATGCTGCACCCCCTTCGCACATTCCGTCGGGCAGCACGAACCGTCGCGGTAGCCACCGCAGCGCTCCTCTTCCGCTCGCCGGAGCACATCCGGCCAGTGCAGACGC
CGCACGTGCGGCAGCCGCAGGTTCGGGATATTGGCACACGTCAGGTCGCCAGATCCTGGATGCAGCAAACCAGCCCGTGCGCATCGCAGGAATCAATTGGTTCGGAT
TCGAAACCGCAAACTATGTCCCGCATGGCCTCTGGAGCCGTGACTATAAGTCGATGATCGACCAAATGAGGTCCCTGGGTTATAACACGATCCGTCTGCCGTACTCA
GATGACATATTCGCAGGAACCGAGCCGGCAAGCATCAATTATTCGGCGGGTATGAATACGGATCTCGCAGGTCTGAACTCGCTCCAGGTGATGGACCGTATCGTCGA
CCACGCCGGCAGTTTCGGAATGAAAGTAATCTTGGATAGGCACCGTCCCGACTCCGCACAGGTCAGTCGGCACTGTGGTATACCTCCGCGGTACCGGAGAGCACGTGGC
TGGCACATCTCAAGTCACTTGCGGCCCGCTACGCGGGCAATGACGCCGTGTGGTAGGTATCGACCTCCACAACGAGCCGCACGACCCGGCATGTTGGGGCTGTGGAGAT
ACCACGAAGGACTGGCGTCTCGCCGCGCAGCGCCGCATTGAGCGCCAATCCGGACCTTCTGATATTCGTCGAGGGGGTGCAGACGGTAGATGGAGT
CTCGGGCTGGTGGGGTGGTAACCTGATGGGAGTGGGACAGTATCCCGTGGAACTGTCTGTGCCGCACAAGGTGGTGTACAGCGCACACGATTACGCAACCAGTGTGG
CACAACAGCCTTGGTTCACGGACAGTTCCTTCCCGGACAATATGCCCGGTGTCTGGGATAAGTATTGGGGCTACATCTTCAAACAGAACATTGCCCCCGTATGGGTA
GGTGAATTCGGAACCACACTGCAGAGTACCACCGACCAGAAAATGGCTCAAGGCCCTGGCGGGACTATCTGCGACCGACAAGCCAGTACGGAGCAGACTCGTTCAGCTG
GACGTTCTGGTCTTGGAATCCCAACTCGGGTGATACAGGAGGTATCCTCAAGGACGATTGGACGAGTGTCGACACACGTCAAGGACGGTAGATGGAGT
CGCCGGACTTCGGTAATGGTGGTGGCGATGACGACACACAGGCCCCGACGGCACCAACAGGACAACCGGTACCAGTGTCTCG
CTGAGTTGGAAGGCAGCATCGGACGACACGAGGGGTGACAGCGTATGACGTCTACCGCGGTAGCACGAAGGCAGGAACCGCGACAGGTACGACGTTCACAGACACGGG
TGTAACCTCGGGTACGAGTTATACCTATACAGTCCGCGCACGAGACGCGGCAGGAAACACGTCCGCCCCCTCGGCATCGGTAACCGCAACCACGACAGGGTCCGGAG
GAAATACCGGTTGTAAAGCCGTGTACACGGAGACTGGGGGTCGGGATTCGGGGTAGACATCACCGTGACGAACACAGGCACCGCCCCGGCAACGAGCTGG
AAGTTGACATGGACCTACGGTGGCTCGCAGAAAATAACGAATATGTGGAACGCAAGCTATACCCAGTCAGGCGCCTCCGTGACCGTAACATCTACAGACTACAATGG
AGGACTCGCGGCAGGGGCACACACCGGCTTCGGTTTCCAGGGAACACCCGCGGCGGGCGCAGTCCCAACCGTGTCCTGTACGCTGAGTTAA

>95 GH9 (SEQ ID NO:31)
ATGCGAAGTTTCCCCCTGCCCGCGCTGAGGAGACGGAGTCGGCGGCCCGGACGTCCCCCTCGGAGCAGTCGCCTTGGCCCTGGCAGTCGGCGCCGGTCTGCTGCTCCC
GTTGTCGCTGCCGGCCGGAGCAGCACCGGCCTTCGACTATGGAGAAGCCTTGCAGAAGTCGGTACTGTTCTACGAGGCCCAGCAATCAGGAAAGTTGCCGGG
ATACGAACAGGGTGAGCTGGCGCGGCGACACGCACTCGACGATGGTAAAGACGCCGGACTGGACCTCACCGGAGGTTGGTATGACGCCGGCGACCACGTAAAGTTC
GGGCTGCCAATGGCATACTCAGCAACGATGCTGGCATGGGTGGCACCGAACAACGCGCCGCGTACGAAGCAAGCGGACAAGCTGCCCCATCTGCGCAATAACTTGCG
TTTCGTAGACGACTATCTGCTGAAGGCGCACCCGTCACCGAATGTCTTGTACGGGACAAGTCGCCTTCCATCATAAGTGGTGGGGACCGGCAGAAGTAA
TGCCGATGAAGCGGCCGGCGTATAAAATAGACGCATCCTGCCCGGGTAGCGACCTGGCGGGTCAGACCGCCGCAGCGCTCGCAAGTTCGTCCATGGTGTTCTCGGAC
AGTGACCCCGCCTACGCCGCAAAATTGATTACACACGCAAAGCAACTGTACACCTTCGCGGACACGTATCGCGGCAAGTACTCGGACTGTATCACGGACGCACAGTC

FIG. 14 (continued)

Example 2 DNA sequences

GTACTACAACTCCTGGAGCGGCTATAATGATGAGTTGGTATGGGGCGCGATCTGGCTTTACAAAGCAACCGGAGACACCGCCTACCTGGCAAAGGCCGAGTCCTATT
ACGACAACCTCTCGACCGAACCGCAGACAACGACGCGATCATATCGCTGGACCTTGTCGTGGGATGACACCTCCTACGGCGCGTATGTCCTTCTCGCACAACTCACG
GGAAAACAGAAGTACATTGACGACGCAAATCGGTGGTTGGACTGGTGGACCGTGGGAGTCAACGGACAGCGCGTGCCCTATAGCCCGGGTGGTCAGGCAGTACTGGA
TAGCTGGGGTAGTCTGCGGTACGCCGCCAACACCGCGTTCGTAGCACTCAGCTACTCCGACTGGCTGACAGGTGACGCAACGCGTAAGGCCCGGTACCACGATTTCG
CCGTGCGCCAGATCGACTATGCACTCGGAGATAATCCGCGAGGATCGTCCTATGTCGTCGGTTTCGGCGAGAACCCACCCACCAAACCGCACCATCGTACGGCGCAC
GGTTCGTGGACCGACCAAATGACCAATCCGGTGGAGACGCGCCACACGCTGTACGGAGCACTGGTAGGCGGACCCTCAGCCCCAGACGATACCTATACAGACGACCG
AGGGAACTACGTCAATAACGAGGTGGCAACCGACTACAACGCGGCCTTCACTGGAGCGTTGGCACGACTGTATGCGGAGTACGGAGGTTCGCCCCTCACCGACTTCC
CTCAGCCGGAAGAGCCCGACGGACCGGAAATGAGCGTCCAGGCATCTGTAAATGCAGCGGGAGCCAACTTCACAGAGGTGAAGGCGTATCTTATTAACCGAAGTGCC
TGGCCAGCACGCGCACTCACAGATGCAAGCGTCCGATATTACTTCACCCTGGAACCGGGAGTCGCCCCGGGAGACATTAGTTTCACGACAAACTATAATCAATGCGG
CGAGGTCACCGGCCCTACGCACCTGACAGGAGATGTCTACTATGCAACCGTCGACTGTTCAGACACAGACATCGCCCCGGCCGGCCAGAGCGCATACCGTAAAGAAG
TGCAGTTCCGCATCTCCAGCGCAGGTGCATGGGATCCTTCCAACGACTGGTCGTATCCGAGCACGGCAACTACCCCCGGAGGTACGCCGGTCGACGCCCCCCATATG
GTACTCCTTGAGGGTTCGGCGCCGCAGTGGGGGACGGCCCCTGATGGAACCGACCCGGGACCAGGTCCGGACCCTACCACAACGCCGGAACCATCCCCGACGCCAGA
CCCAACCGATACACCCGACCCGGAACCTGGAGCATGCGATGTCACCTACCGAGTGTCGCAGGCATGGGGTACAGGGTTCACCGCGGACGTCACAGTCAAGAATACGG
GACCGACCCCCCTCGACGGATGGCAGCTTGCATTCGACTTCCAGGGAGCCGAGAGTGTATCGAACGCGTGGAACGCCACCGCGACGCAGAGTGGAACTAGGGTGACC
CTCAAGAACGCAGGTCACAACGGCTCGGTGCCGGCAGGTGGTTCCGCCTCGTTCGGCTTCCAGGCGAACGGGGCCCCCGGAGCAGACCCGCATAGTTTCACATTGAA
CGGAAAGGAATGTGGTTGA

>95 GH12 (SEQ ID NO:32)

ATGACAGGCCGGCCGCTGCCGGCATTGGCAGGAGCGGCAGCCGCACTGGTCCTGGCGGCGGCAAGCATGCTGACCGGAGCGAGCTCCGCAAGCGCGTCGCCGGTGAC
CGATTGTACACCGTGGGGTACAACGGAGCTCCTCGGTGGGGAGTACTTGTATCAGCAGAACGAGTGGAACTCGGACAGCGAACAATGTGTCGGAGTGGACCCGGACA
CCGGAGCCTGGAGCGTAACAACAAGCAGCTTCAATCTTCCCACAAACGGCGCACCAGCCACGTACCCGAGCAGCTATAAGGGATGCCACTGGGGGGCATGTACCTCG
GATTCTGGACTGCCGCTCCGCGTGGACGAGTTGGGATCAGTACATACAGACTGGTCGACCACACAGGTAGGCTCCGGTGCCTATAATGTGAGTATGGACGTCTGGTT
TAACAGTGCACCTGTAACGGATGACCAGCCGGACGGCACGGAACTGATGATCTGGATGAACCACCGCGGTGGAGTGCAGCCCATTGGAAGCCGTACGGCCACAGTCC
AGCTCGATGGTCGCACGTGGGACGTATGGACCGGACCCGGCGCATCGGGATGGAAGGTCATCAGTTACGTCTTGCAGGGCGGAGCGACCGAGCTCACAGGGTTCGAT
GTGAAGTCGTTGATCGACGACGGAGTGGGTCGTGGCCAAATAGACCCGGCCCATTATCTCATCGACGCAGAGGCCGGATTCGAGATCTGGCAGGGTGGCCAGGGGCT
GGGTATGAAAGAGTTCAGCTTCGAGGCCAGCGCAGGAACCGACGGTGGCGATGACGGAGGCGACGGCGATCCGGGCGGCGGAGGCACCACAGGAGCACTCAAGGCCC
AGTACAAAAATAACGATTCCAGCGCGACGGACAATCAGATACGCCCAGGCCTGCAGCTCGTGAATACCGGATCCACAGCTGTCGACCTGTCTACTGTGAAGCTGCGG
TACTGGTTCACCCCCGAAAGTGGCGCGGCGGGTTTCGGCACGGCCTGTGATTATGCAGTCGTCGGTTGTGGAAACGTCACGCACACGGTAAAGCAAGCAGGGACGGC
AGCCGGCGCATCACACTACTTGGAGGTGGGTTTCACGGGCGGATCGCTGGCCCCGGGTGCATCGACCGGTGAAATTCAGCTGCGATTCAACAAGTCGGATTGGTCGG
CGTTCGACGAAGCCGACGACTACAGTCGTGCAGCGAACACGGCGTTCACCGACGCATCGAAGGTGGGTGTCTACGTGAATGGAGCATTGTCAAGCGGTACAGCGCCG
TGA

FIG. 14 (continued)

METHOD OF CREATING INDUSTRIAL STREPTOMYCES WITH CAPABILITY TO GROW ON CELLULOSIC POLYSACCHARIDE SUBSTRATES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application No. 62/318,399 filed on Apr. 5, 2016, the contents of which are incorporated by reference in its entirety.

STATEMENT REGARDING FEDERALLY FUNDED RESEARCH

This invention was made with government support under DE-FC02-07ER64494 awarded by the US Department of Energy. The government has certain rights in the invention.

BACKGROUND

Cellulose is the most abundant organic polymer on Earth and represents a vast source of renewable energy. Most of this energy is stored in the recalcitrant polysaccharide cellulose, which is difficult to hydrolyze because of the highly crystalline structure, and in hemicellulose, which presents challenges because of its structural diversity and complexity. Plant cell walls, approximately composed in pinewood of lignin (30% by weight), hemicellulose (glucomannan, 20%, arabinoxylan, 10%), and crystalline cellulose (40%), present a major barrier to its efficient use. In terrestrial ecosystems, cellulolytic microbes help drive carbon cycling through the deconstruction of biomass into simple sugars. The deconstruction is largely accomplished through the action of combinations of secreted glycoside hydrolases (GHs), carbohydrate esterases (CEs), polysaccharide lyases (PLs), and carbohydrate binding modules (CBMs). Consequently, organisms from many lignocellulose-rich environments and their enzymes are being studied for new insights into overcoming this barrier.

In order to obtain the hydrolysis of crystalline cellulose, enzymes must cleave three types of glycosidic bonds. These enzymes are endocellulases, which cleave beta-1,4 glycosidic bonds that reside within intact cellulose strands in the crystalline face, non-reducing-end exocellulases, which remove cellobiose units from the non-reducing end of cellulose strands, and reducing-end exocellulases, which remove glycosyl units from the reducing-end of a cellulose strand. The endocellulolytic reaction is essential because it creates the non-reducing and reducing ends that serve as the starting point for exocellulolytic reactions. The exocellulolytic reactions are essential because they remove glycosyl groups in a processive manner from the breakages in the cellulose strand introduced by the endocellulases, thus amplifying the single initiating reaction of the endocellulases.

Although a large number of *Streptomyces* species can grow on biomass, only a small percentage (14%) have been shown to efficiently degrade crystalline cellulose. Furthermore, the secreted cellulolytic activities of only a few species have been biochemically characterized, and still fewer species have been examined to identify key biomass degrading enzymes. For example, *Streptomyces reticuli* is one of the best-studied cellulose- and chitin-degrading soil-dwelling *Streptomyces*; functional analyses of several important cellulases and other hydrolytic enzymes have been reported.

Furthermore, polysaccharide monooxygenase (PMO) activity with cellulose was identified using the CBM33 protein from *Streptomyces coelicolor* (Forsberg, et al., 2011), which suggests *Streptomyces* may use both hydrolytic and oxidative enzymes to deconstruct biomass. With the tremendous amount of sequence data collected in the past few years, and despite the view that *Streptomyces* make important contributions to cellulose degradation in the soil, genome-wide analyses of cellulolytic *Streptomyces* are only recently being reported. For example, see Book, et al, Appl Environ Microbiol 80:4692-4701, 2014.

In addition to their putative roles in carbon cycling in the soil, *Streptomyces* may also potentiate biomass deconstruction in insects through symbiotic associations. Recent work has identified cellulose degrading *Streptomyces* associated with the pine-boring woodwasp *Sirex noctilio*, including *Streptomyces* sp. SirexAA-E (ActE) (Adams, et al., 2011). *S. noctilio* is a highly destructive wood-feeding insect that is found throughout forests in Eurasia and North Africa and is spreading invasively in North America and elsewhere. While the wasp itself does not produce cellulolytic enzymes, evidence supports the role of a symbiotic microbial community that secretes biomass-degrading enzymes to facilitate nutrient acquisition for developing larvae in the pine tree.

The white rot fungus, *Amylostereum areolatum*, is the best-described member of this community, and the success of *Sirex* infestations is thought to arise from the insect's association with this cellulolytic fungal mutualist. However, work with pure cultures has suggested that ActE and other Sirex-associated *Streptomyces* are more cellulolytic than *A. areolatum*.

Needed in the art are improved compositions and organisms for digestion of lignocellulosic materials. Specifically, there is a need for industrialized *Streptomyces* that can accept a greater complexity of less-expensive feedstocks.

DESCRIPTION OF THE FIGURES

This patent application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIGS. **1**A-**1**C are a demonstration of highly cellulolytic *Streptomyces* strains that contain suites of enzymes lacking in industrialized strains that are necessary to consume cellulose as a food source. (A) is a model for enzymatic hydrolysis of cellulose using up to five enzymes. (B) is an example of a cellulolytic *Streptomyces* and a non-cellulolytic *Streptomyces* when cultured on filter paper as the sole carbon source. The cellulolytic *Streptomyces* is capable of growth and degradation of filter paper. (C) is an example of a non-cellulolytic *Streptomyces* cultured with four different carbon sources, and the strain is only capable of growth on glucose and cellobiose.

FIGS. **2**A-**2**B show standard cloning techniques that we used to produce synthetic operons containing cellulolytic genes from ActE to enable non-cellulolytic *Streptomyces* strains to produce functional cellulase enzymes. (A) is a diagram showing an example synthetic operon with promoter, genes, RBS (ribosome binding sequences), and terminator sequences. (B) shows a mechanism for cloning the genes via PCR from genomic DNA and assembling using Gibson assembly to create an operon like FIG. **2**A. PCR from genomic DNA is one way to generate genetic material for construction of these operons. Another way is DNA synthesis (including codon optimization) as in FIG. **4**.

FIG. **3** discloses three optimized synthetic operons designed to express cellulase enzyme sets from three insect-associated *Streptomyces* strains that were generated by artificial gene synthesis for heterologous expression in industrialized, non-cellulolytic *Streptomyces* hosts. ActE (*Sirex* woodwasp), *Streptomyces* sp. DpondAA-B6 (*Dendroctonus ponderosae* mountain pine beetle), and *Streptomyces* sp. LaPpAH-95 (*Petalomyrmex phylax* ant) are *Streptomyces* strains isolated from their respective insect associations and are characterized by high natural cellulolytic abilities.

FIG. **4** is a schematic diagram of the gene sequences for synthetic operons that were optimized for highest predicted expression in industrialized *Streptomyces* host strains.

FIG. **5** is a summary graph of the activity of secretomes from industrial *Streptomyces* expressing single ActE cellulases or gene cassettes as described above and in the Examples.

FIG. **6** is a SDS-PAGE of *S. lividans* secretomes harboring combinatorial or control cellulolytic operons. Red labels represent secretomes with the highest activity on cellulose.

FIG. **7** is a diagram of the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on amorphous cellulose (PASO). EV is an empty vector control containing pSET190 plasmid without cellulase genes. pACTE contains 5 ActE cellulase genes, pActE-B contains 5 ActE cellulases plus the B6 GH12 cellulase, pB6 contains 5 DpondAA-B6 cellulases, and p95 contains 6 LaPpAH-95 cellulases.

FIG. **8** discloses the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on crystalline cellulose (filter paper). Samples are as described in FIG. **7**.

FIG. **9** discloses the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on lichenan. Samples are as described in FIG. **7**.

FIG. **10** is a plot of the correlation between the days required for strains to break filter paper in vivo and in vitro cellulase activity of secretomes of *S. lividans* containing combinatorial (blue) or control cellulolytic operons (red).

FIG. **11** is a diagram disclosing the presence of genes assigned from direct Illumina sequencing of *S. lividans* harboring combinatorial cellulolytic operons.

FIG. **12** is a diagram of combinatorial gene operons produced for Example 2.

FIG. **13** is a document listing the protein sequences examined in Example 2.

FIG. **14** is a document listing the DNA sequences examined in Example 2.

DESCRIPTION OF THE INVENTION

In one embodiment, the present invention is an optimized set of enzymes useful to create an industrial *Streptomyces* with the capability to grow on cellulosic polysaccharide substrates.

In General

The Examples below disclose several embodiments of the present invention, which is a general strategy for providing an optimized set of heterologous genes (encoding an optimized set of enzymes) for transformation into a host *Streptomyces* species.

As disclosed in FIG. **1**, one suitable enzyme cassette comprises (1) a non-reducing-end exoglucanase from the GH6 family, (2) endoglucanase from the GH5 and/or GH12 families, (3) an endoglucanase from the GH9 family, (4) an auxiliary activity enzyme from the AA10 family, and (5) a reducing-end exoglucanase from the GH48 family. The preferred enzyme cassette requires two different endoglucanases because these distinct enzyme fold families provide variations in catalytic properties that contribute to enhanced cellulolytic capability. An AA10 enzyme uses copper(II) ions, reducing agents and O2 gas to degrade cellulose in an oxidative manner that is complementary to the hydrolytic reactions carried out by the GH family enzymes. In a preferred embodiment, the genes in the cassette are not from a single species.

A second embodiment of the present invention is a heterologous gene cassette wherein at least two of the enzymes described in (1)-(5), above, are present in the cassette. Preferably, the cassette comprises the endoglucanase from the GH9 family, preferably isolated from *Streptomyces* LaPpAH-95, and an endoglucanase from the GH5 and/or GH12 families, preferably the GH12 endoglucanase isolated from *Streptomyces* DpondAA-B6. In another embodiment, the cassette comprises ActE-GH5, B6-GH9, and B6-GH12, as described below in the Examples.

By "the capability of growing on cellulosic polysaccharide substrates," we mean that the transformed organism is better able to grow on biomass, preferably at least one of the following substrates: cellulose, hemicellulose, paper, or wood products. Biomass is generally defined as organic materials, such as plant matter and manure, which have not become fossilized and can be used as a fuel or energy source. Of particular importance to the present invention is biomass composed of plant material, vegetation, or agricultural waste. Wood is the largest biomass energy source. Forest residues (such as dead trees, branches and tree stumps), yard clippings, and wood chips are all examples of wood biomass. Non-wood biomass includes plant or animal matter that can be converted into fibers or other industrial chemicals, including biofuels. Non-wood biomass can be grown from numerous types of plants, including miscanthus, switchgrass, hemp, corn, poplar, and willow.

Other substrates include corn stover, prickly pear cactus cladodes, kelp, sorghum, straw, poplar, eucalyptus, pine, sugarcane bagasse, cotton, bamboo, nut shells, bark, sawdust, wood chips, and paper mill waste. In the Examples below, the model cellulosic polysaccharide substrate is phosphoric acid-swollen cellulose (PASO). The ability of an organism to degrade this substrate would be useful to understand whether a recombinant organism is within the scope of the present invention.

We specifically envision that the present invention will be useful for treated (or pretreated) and untreated biomass. Preferably, the organism is able to break down insoluble, recalcitrant polysaccharides such as cellulose, hemicellulose, and mixed polysaccharide biomass to produce small oligomeric and/or monomeric, soluble sugars that it can import for use as a nutritional carbon source. This in turn is utilized by the cell for the increased production of cellulolytic enzymes, increased cell growth density, and/or for the production of other value-added metabolites. Cellulolytic activity may be measured as described below in the Examples or by other methods known to those of skill in the art.

By "heterologous," we mean that the genes in the cassette do not naturally occur in the host species.

Specific Combinations of Enzymes

The Examples below disclose particularly advantageous combinations of heterologous enzymes, preferably presented to the host *Streptomyces* as an operon or cassette. In one embodiment, each operon typically comprises at least two members selected from a GH6 gene, a PMO gene, a GH48 gene, a GH5 gene and either (a) a GH9 gene, (b) a

GH9 gene and a GH12 gene or (c) a GH12 gene. Many of the CAZy (Carbohydrate-Active enZYmes database) classes (for example, GH5, GH6, etc.) contain multiple types of enzymes, unified by their general type of reaction and diversified by substrate specificity and product formation. Table 1, below, describes preferred members of the classes. Preferably, the genes are obtained from more than one species.

TABLE 1

CAZy gene class	Enzyme name	Enzyme Commission (EC) #	Reaction mechanism	GH catalytic proton donor	GH catalytic nucleophile/ base	protein fold clan	structural class	Add'l specs
GH5	endo-beta-1,4-glucanase	EC 3.2.1.4	Retaining hydrolysis	Glu	Glu	GH-A	(beta/alpha) 8	
GH6	non-reducing end cellobiohydrolase	EC 3.2.1.91	Inverting hydrolysis	Asp	Asp			processive
GH9	endoglucanase	EC 3.2.1.4	Inverting hydrolysis	Glu	Asp		(alpha/alpha) 6	
GH12	endoglucanase	EC 3.2.1.4	Retaining hydrolysis	Glu	Glu		beta-jelly roll	
GH48	reducing-end cellobiohydrolase	EC 3.2.1.176	Inverting hydrolysis	Glu		GH-M	(alpha/alpha) 6	processive
AA10	copper-dependent lytic polysaccharide monooxygenase (LPMO)		Oxidative	Not applicable	Not applicable			previously called CBM33, PMO or LPMO

In one embodiment of the invention, the genes encoding the CAZy classes are selected from highly-cellulolytic *Streptomyces* strains, such as the insect-associated strains *Streptomyces* sp SirexAA-E (ActE), *Streptomyces* DpondAA-B6, and *Streptomyces* LaPpAH-95. Preferred embodiments are listed in Example 2. The paragraph below includes each of the enzymes in Example 2 listing their NCBI reference numbers. This reference number can be searched at the NCBI website to find the exact protein sequence used to create synthesized/optimized DNA. FIG. **13** is a document listing the protein sequences for the Example 2 experiments (SEQ ID NO:1 and 3-17) and FIG. **14** is a document listing the DNA sequences after optimization (SEQ ID NO:2 and 18-32).

Organism	CAZy Family	NCBI Reference Number
ActE	GH48	AEN08183.1
ActE	GH5	AEN08423.1
ActE	GH6	AEN08184.1
ActE	GH9	AEN11565.1
ActE	LPMO	AEN11025.1
DpondAA-B6	GH12	WP_028441901.1
DpondAA-B6	GH48	WP_028441980.1
DpondAA-B6	GH6	WP_078552084.1
DpondAA-B6	GH9	WP_028439469.1
DpondAA-B6	LPMO	WP_028441526.1
LaPpAH-95	GH12	WP_018105227.1
LaPpAH-95	GH48	WP_018105228.1
LaPpAH-95	GH5	WP_018104961.1
LaPpAH-95	GH6	WP_026171800.1
LaPpAH-95	GH9	WP_018105029.1
LaPpAH-95	LPMO	WP_018099987.1

In another embodiment of the invention, the genes are selected from *Streptomyces* clades I and III (the cellulolytic clades). For more information, see Book A J, Lewin G R, McDonald B R, Takasuka T E, Wendt-Pienkowski E, Doering D T, Suh S, Raffa K F, Fox B G, Currie C R. 2016. Evolution of high cellulolytic activity in symbiotic *Streptomyces* through selection of expanded gene content and coordinated gene expression.

In three specific preferred combination, the gene cassettes are as disclosed in FIG. **3**.

The enzyme combination of the present invention is optimally presented to the *Streptomyces* as a gene cassette, preferably under the control of a single constitutive promoter, such as the ermE* promoter described below. Other useful elements include the use of ribosomal binding site (RBS) sequences. A successful operon must have a promoter in order to initiate transcription of the subsequent genes. Many promoters could substitute for the ermE promoter used in the Examples. We chose one of the most commonly-used promoters for genetic engineering in these organisms. A terminator at the end is desirable to increase the stability of the transcript and to allow RNA polymerase to finish a transcript and begin a new one. Likely many different kinds of terminators could substitute. Many studies do not include a terminator and generate acceptable results. Every gene requires an RBS for the ribosome to bind the transcript and initiate translation at the next start codon. Random sequence upstream of a gene will initiate ribosome binding at an extremely low rate, so sequence that is tailored to attract ribosomes is essential for efficient enzyme production.

In a preferred version of the present invention, the gene order is the same as that disclosed below in the Examples. We chose a gene order based on wild-type expression of the enzymes in the ActE organism (from highest expressed to lowest) and then continued that pattern with the homologous genes from B6 and 95 strains. However, this gene order does not exist in nature. The preferred gene optimization is designed to minimize a gene order effect by altering repetitive sequence that could affect translation of each gene and neighboring genes.

In a preferred version of the present invention, the genes are subjected to a gene optimization strategy to substantially optimize enzyme expression compared to the wild-type sequences. In the case of wild-type genes that don't appear

to express in the host strain, "substantially" optimized means that expression is high enough to be clearly detectable from a 10 uL load on a Coomassie Stained SDS-PAGE gel after 10-fold concentration of cell supernatant. The minimum level for this detection is approximately 10 ug/mL (assuming 100 ng comprises a clearly detectable protein band). A substantial improvement in expression of a wild-type gene that does express in the host at a low level would be at least two times higher that this low threshold.

One typical optimization would be to change any alternative start codons (TTG, GTG, or CTG) to the standard ATG start codon. Another optimization would alter codon usage to remove repetitive sequence that is predicted to produce transcript hairpins which can interfere with translation. One may also wish to modify codon usage to substitute rare codons (e.g. TTA) to preferred codons or to alter codon usage to facilitate artificial gene synthesis. These modifications are predicted to substantially optimize enzyme expression compared to the wild-type sequences.

One may wish to consult gene optimization strategies utilizing the GeneDesign tool (http://genedesign.jbei.org), the in-house JGI Sequence Polishing Library tool, or manual manipulations to accomplish the above objectives. The cassettes of the present invention are then introduced into a host *Streptomyces* in any suitable manner. One of skill in the art would understand that there are numerous suitable ways to achieve this result. One suitable reference would be the book Practical *Streptomyces* Genetics by Kieser T, Bibb M J, Buttner M J, Cjater K F, and Hopwood D A (2000). The important techniques include protoplast transformation and conjugation from *E. coli*. There are other techniques as well, all described in chapter 10, "Introduction of DNA into *Streptomyces*".

Suitable *Streptomyces* Host Strains

As described below, particularly suitable *Streptomyces* strains are *S. lividans* or *S. venezuelae* strains. However, other commercially important *Streptomyces* are *S. coelicolor* and *S. griseus*. Other suitable strains include *Streptomyces clavuligerus, Streptomyces hygroscopicus*, and *Streptomyces viridochromogenes*, and *Streptomyces avermitilis*.

EXAMPLES

Example 1

Optimized Set of Enzymes

FIGS. **1** through **5** disclose a set of experiments designed to discover an optimized set of enzymes useful to create an industrial *Streptomyces* with the capability to grow on cellulosic polysaccharide substrates.

FIG. **1** is a demonstration of an essential suite of enzymes from highly cellulolytic *Streptomyces* strains that are necessary to consume cellulose as a food source. These enzymes are lacking in industrialized strains such as *Streptomyces griseus, Streptomyces venezuelae* and others. Referring to FIG. **1**, (A) is a schematic showing a single cellulose chain being deconstructed into cellobiose units (composed of two beta-1,4-linked glucose units) by the critical enzymes classes that aid in cellulose consumption by natural highly cellulolytic *Streptomyces* strains. (B) demonstrates that the wood wasp-associated *Streptomyces* sp. SirexAA-E (ActE) consumes a 1×10 cm cellulose filter paper strip as the sole carbon source in under 5 days, while the industrialized *Streptomyces griseus*, lacking the critical suite of functional enzymes, is unable to efficiently grow. (C) depicts industrialized *Streptomyces venezuelae* strain readily growing when glucose or cellobiose is the sole carbon source but lacking functional celluloytic enzymes to efficiently grow using cellulose or filter paper as the sole carbon source, as evidenced by the absence of mycelial clumping.

FIG. **2** shows standard cloning techniques that we used to produce synthetic operons containing cellulolytic genes from ActE to enable non-cellulolytic *Streptomyces* strains to produce functional cellulase enzymes. Referring to FIG. **2**, (A) is a diagram showing an operon designed to express five specific ActE cellulase genes in *Streptomyces* [Gene ID number (CAZy enzyme class)]: SACTE_0237 (GH6); SACTE_3159 (LPMO); SACTE_0236 (GH48); SACTE_0482 (GH5); and SACTE_3717 (GH9). The five genes are critical for the cellulolytic capabilities of ActE based on proteomic and transcriptomic analyses and have non-redundant biochemical functions. The synthetic operon also contains a constitutive high-expression promoter (P21p or ermE*, Siegl et al., 2013), ribosome-binding-site sequences (from Siegl et al., 2013 or calculated for each gene as in Espah Borujeni et al., 2014), and the synthetic terminator BBa_B1006 (Cambray et al., 2013). (B) shows the result of ActE cellulase genes amplified with complementary overlapping sequences and assembled with New England Biosciences NEBuilder HiFi DNA Assembly to produce complete synthetic operons. The arrangement of these genes does not exist in nature, as they are under the control of different promotors, have different RBS sequences, and can be transcribed in opposite directions. The arrangement we've created takes advantage of placing the most highly expressed natural protein as the first gene.

FIG. **3** discloses optimized synthetic operons designed to express cellulase enzyme sets from three different insect-associated *Streptomyces* strains. These enzyme sets were generated by artificial gene synthesis for heterologous expression in industrialized, non-cellulolytic *Streptomyces* hosts. ActE (Sirex woodwasp), *Streptomyces* sp. DpondAA-B6 (*Dendroctonus ponderosae* mountain pine beetle), and *Streptomyces* sp. LaPpAH-95 (*Petalomyrmex phylax* ant) are *Streptomyces* strains isolated from their respective insect associations and are characterized by high natural cellulolyic abilities. Transcriptomic and/or proteomic analyses of these strains revealed high-abundance cellulases of CAZy enzyme classes (http://cazy.org): GH6; AA10 (also abbreviated as LPMO or PMO); GH48; GH5; GH9; and GH12. Synthetic operons were designed to include the ermE* promoter, gene sequences with optimized RBS spacers (calculated by Espah Borujeni et al., 2014), and the synthetic terminator BBa_B1006 (Cambray et al., 2013). The complete synthetic operons were synthesized as a service by the Joint Genome Institute (JGI) and inserted into the pSET152 vector for integration into industrialized host strains *Streptomyces lividans* and *Streptomyces venezuelae*. (See Bierman et al, 1992, Gene 116:43-49, for information about pSET152.)

FIG. **4** is a schematic diagram of the gene sequences for synthetic operons that were optimized for highest predicted expression in industrialized *Streptomyces* host strains. The gene sequences specified in FIG. **3** were subjected to a gene optimization strategy to 1) change any alternative start codons (TTG, GTG, or CTG) to the standard ATG start codon, 2) alter codon usage to remove repetitive sequence that is predicted to produce transcript hairpins which can interfere with translation, 3) modify codon usage to substitute rare codons (e.g. TTA) to preferred codons, and 4) alter codon usage to facilitate artificial gene synthesis. These modifications are predicted to substantially optimize enzyme expression compared to the wild-type sequences. The gene optimization strategy utilized the GeneDesign tool

(http://genedesign.jbei.org), the in-house JGI Sequence Polishing Library tool, and manual manipulations to accomplish the above objectives.

As an example of the optimization strategy, ActE genes SACTE_0237 (GH6), SACTE_3159 (LPMO), SACTE_0236 (GH48), SACTE_0482 (GH5), and SACTE_3717 (GH9) are depicted with shaded lines (referring to FIG. **4**) indicating the positions of nucleotide substitutions, the percent identity between wild-type and optimized sequences, and the change in GC nucleotide content after optimization. See Exhibit D of Ser. No. 62/318,399 for exemplary optimized gene sequences.

FIG. **5** is a summary graph of the activity of secretomes from industrial *Streptomyces* expressing single ActE cellulases or gene cassettes as described above. Expression of single genes or the entire gene cassette is under control of a single constitutive ermE* promoter (Siegl et al., 2013). The importance of the cellulolytic genes in creating an active secretome was established by control experiments (FIG. 5, A-F) using wild-type (WT) ActE (A.), *S. lividans* (C.), and *S. venezuelae* (E.) or these same strains transformed with empty pSET152 vector lacking cellulolytic genes (SET) ActE (B.), *S. lividans* (D.), and *S. venezuelae* (F.).

Secretomes were prepared in the following manner. 50-mL cultures of individual ActE, *S. lividans* or *S. venezuelae* WT, SET, individual cellulolytic gene, or cassette transformants were grown in YEME (yeast extract/malt extract media, Kieser et al.) (medium with 0.05% antifoam A for 4 d at 28° C. with shaking at 275 rpm. Cultures were treated with protease inhibitor cocktail (Roche complete EDTA-free), centrifuged twice for 30 minutes at 4° C. and 4,300×g, and vacuum-filtered through a glass pre-filter followed by a 0.2 micron PES filter.

The filtrates were concentrated at 4° C. using Vivaspin Turbo-15 PES 10,000 MWCO centrifugal concentrators (Sartorius Stedim) to 2-3% of the starting volume, and exchanged three times using 10 mM MOPS, pH 7, 50 mM NaCl to lower reducing sugar levels in the media. Desalted secretomes were concentrated to approximately 2 mL volume and analyzed by SDS-PAGE to determine the secreted protein expression profile. Total protein concentration was measured using a Bio-Rad protein assay.

Cellulolytic activity was measured using the 3,5-dinitrosalicylic acid assay (DNS; Miller, 1959) to detect reducing sugar products. Briefly, 20 pg of total secretome protein was combined with 500 pg of phosphoric acid-swollen cellulose (PASC), 10 mM MES, pH 6, 5 mM ascorbate, and 0.025% sodium azide in a volume of 50 μL. Duplicate reactions were incubated at 42° C. for 22 h with agitation. Individual secretomes, prepared as described above, were used in all cellulolytic activity assays with the exception of PMO/5/6/9/48, which contained roughly equimolar mixtures of secretomes G., H., I., J., and K. for a total load of 20 pg protein. The ActE secretome positive control consists of 20 pg of purified ActE secretome harvested from a 6 d growth of ActE on 0.3% PASC in M63 defined medium.

Cellulolytic activity assays were briefly centrifuged and 30 μL of the soluble fractions were combined with 60 μL of DNS reagent in a microplate alongside glucose concentration standards, heated to 95° C. for 5 min, then cooled to 4° C. Reactions were diluted 7.5-fold with water and the absorbance at 540 nm was measured using a Tecan plate reader. The concentration of reducing sugar was determined from a linear plot of standard absorbance versus concentration. The percentage conversion was determined following background correction from no-substrate and no-enzyme controls, and plotted as percentage of the mass of reducing sugar released per mass of polysaccharide substrate.

Referring to FIG. **5**, *S. lividans* or *S. venezuelae* strains were created that contained integrated copies of single ActE cellulase genes SACTE_0236 (GH48 reducing-end cellobiohydrolase, G), SACTE_0237 (GH6 non-reducing end 1,4-beta cellobiohydrolase, H), SACTE_3159 (AA10 lytic polysaccharide monooxygenase PMO, I), SACTE_0482 (GH5 endoglucanase, J), or SACTE_3717(GH9 endoglucanase, K). (By "integrated," we mean that organisms contained a single copy of the gene inserted into the chromosome.) Addition of single genes gave a more active secretome than observed in WT or SET versions of *Streptomyces lividans*. Also, combination of approximately equal amounts of the five secretomes containing individual enzymes gave a synergistic increase in secretome activity over that obtained by individual enzymes (L. PMO/5/6/9/48) in digestion of PASC. This combination of enzymes, produced in industrial strain *Streptomyces lividans*, has 85% of the PASO conversion ability of the natural highly cellulolytic secretome produced by ActE, U).

Cassettes consisting of five ActE cellulase genes (cassette A), 5 Dpond-AA B6 genes (cassette B), a cross-species combination of 5 ActE cellulase genes plus the Dpond-AA B6 GH12 endoglucanase gene (cassette AB), or single species combination of 6 LaPpAH-95 genes (cassette 9) were also investigated. Expression of the entire gene cassette is under control of a single constitutive ermE* promoter (Siegl et al., 2013). Each gene in the cassette is preceded by an optimized ribosome-binding site (RBS). The cassettes were tested in *Streptomyces lividans* and *Streptomyces venezuelae*, two industrial *Streptomyces* strains that otherwise lack the ability to grow on cellulose.

The combination of cassette and industrial *Streptomyces* strain gave different results. All cassettes imparted the ability to degrade cellulose above that observed in the VVT and SET strains, demonstrating the ability to transfer a natural cellulolytic ability into an industrial strain. The cellulolytic activity of the secretome produced from the cassette was equivalent to that obtained by the more complicated process of expression of single proteins and remix into a multi-enzyme secretome. Moreover, the activity of the secretomes produced from the cassettes was comparable to the PASO conversion ability of the natural highly cellulolytic secretome produced by ActE.

The potential for other optimizations arising from combination of cassettes and *Streptomyces* strains is suggested by FIG. **5**. For example, the A and AB cassettes gave strong activity when transformed into *Streptomyces venezuelae* (Q. and R.), but lesser (albeit considerably above background) activity when transformed into *Streptomyces lividans* (M. and N.). In contrast, cassettes B and 9 gave comparable, high activity in both industrial strains (compare O. and P. with S. and T.)

Example 2

Combinatorial Library

FIGS. **6-11** describe a set of experiments designed to explore a minimal combination of genes required for enhanced cellulolytic activity. A combinatorial library was formed and examined.

Cassette Design

Synthetic operons were designed to contain one gene copy for the enzyme classes GH6, LPMO, GH48, and GH5 and with either a GH9 or a GH12, or both. Synthetic operons

contain ribosome binding sequences (RBS) preceding each gene (e.g., see (1) for de novo RBS prediction), a promoter sequence (e.g., the constitutive promoter ermE*p (2, 3)) preceding the first gene, and a terminator sequence following the last gene. Gene sequences may be optimized for codon usage (e.g., (4)).

A combinatorial library was designed using 16 highly-expressed cellulases from three cellulolytic isolates: *Streptomyces* sp. SirexAA-E (ActE), *Streptomyces* sp. DpondAA-B6 (B6), and *Streptomyces* sp. LaPpAH-95 (95). The set of ActE genes contains GH6, LPMO, GH48, GH5, and GH9 genes. The set of B6 genes contains GH6, LPMO, GH48, GH12, and GH9 genes. The set of 95 genes contains GH6, LPMO, GH48, GH5, GH9, and GH12 genes. Each gene sequence was synthesized de novo and assembled using Gibson assembly (5) to create a library with every possible combination of GH6-LPMO-GH48-GH5-GH9-GH12. In all, 324 (3×3×3×2×3×2) combinations are possible. Each member of the combinatorial library includes RBS sequences, the ermE*p promoter, and a terminator sequences as described above and is inserted into the cloning site of the pSET152 plasmid.

Combinatorial Library Construction

A DNA library containing each of the 324 synthetic operon combinations was prepared at an equimolar concentration. *Streptomyces lividans* 1326 protoplasts were prepared according to page 56 of (8) and transformed with the DNA library according to page 232 of (8). The spores from ~3,000 unique transformants were harvested and stored in 35% glycerol at −80° C. Spores were germinated at 30° C. with shaking for 4 hours in 2×YT medium (2×yeast extract/tryptone media, Kieser et al.), then centrifuged and resuspended in M63 minimal medium before being spread on M63 (minimal media, see Balows A. The Prokaryotes: A Handbook on the Biology of Bacteria. 2nd Ed, New York: Springer-VErlag: 1992) minimal agar containing 0.5, 1, 1.5, or 2% SigmaCell cellulose as the sole carbon source and 50 μg/mL apramycin. (SigmaCell cellulose is a purified highly crystalline form of cellulose that presents a formidable challenge as a growth substrate.) Exceptional strains were chosen based on larger colony size, pigmentation, and/or presence of spores, which were then cultured on IWL4 agar with 50 μg/mL apramycin and spores collected after 14 days to 35% glycerol at −80° C.

Filter Paper Screening

Spores from exceptional strains were added to 2×YT with 50 μg/mL apramycin and grown for 3 days at 30° C. with shaking. 200 μL of each culture was added to 5 mL of M63 media with a 1×10 cm Whatman paper strip as the sole carbon source. After growth at 30° C. with shaking, the filter paper strip from 20 exceptional strains broke within 7-13 days, which compares to >30 days for VVT *S. lividans* or *S. lividans* transformed with pSET152 empty vector.

Secretome Activity Assay

A. Culture Growth Conditions

Fifty mL of 2YT media containing 50 μg/mL apramycin were inoculated from spore stocks and grown in 250 mL Erlenmeyer flasks containing springs to break up mycelial growth at 30° C. for 66 h.

B. Secretome Harvest

Cultures were transferred to 50 mL conical tubes and centrifuged at 4,000×g for 15 min at 4° C. in a swinging bucket rotor. Supernatants were vacuum filtered through 47 mm-diameter, 0.22-micron PES filters and were then concentrated using 10,000 MWCO PES-membrane spin concentrators (Sartorius Vivaspin Turbo 15) until each secretome was ~1.5 mL. The volume was readjusted to 15 mL using 10 mM MOPS pH 7, 50 mM NaCl, and the secretomes were reconcentrated to ~1.5 mL. Buffer exchange was repeated three times, ending with a final concentration of ~1.2 mL/secretome.

C. Total Protein Analysis

i SDS-PAGE: 8 μL of each secretome was loaded onto a 4-20% acrylamide SDS-PAGE gel after heating to 95° C. 2 min in the presence of SDS and β-mercaptoethanol. The gel was imaged using tryptophan fluorescence imaging (Bio-Rad GelDoc EZ imaging system with Stain-Free SGX Criterion gel; see FIG. **6**). FIG. **6** is an SDS-PAGE of *S. lividans* secretomes harboring combinatorial or control cellulolytic operons. Red labels represent secretomes with the highest activity on cellulose.

ii BCA assay: Total protein in each secretome was measured using a standard bichinchonic acid (BCA) micro-assay (Thermo/Pierce) on 5-fold diluted secretomes in water with a bovine serum albumin standard curve.

iii Mass spectroscopy: Pellets from methanol (MeOH) precipitation of extracellular protein samples were resuspended and trypsin digested in urea, tris(2-carboxyethyl) phosphine (TCEP), chloroacetamide buffer overnight. Each sample was desalted and peptides separated over a 75 μm i.d. 30 cm long capillary with an imbedded electrospray emitter and packed with 1.7 μm C18 BEH stationary phase. Eluting peptides were analyzed with an Orbitrap Fusion Lumos in data dependent top 1 second mode. Raw files were analyzed using MaxQuant 1.5.2.8, searching for predicted fragments from the 16 cellulase sequences.

TABLE 2

Mass spectral counts of selected *S. lividans* secretomes containing combinatorial or control cellulolytic operons. DPondAA-B6 GH9 and GH12 were the predominant cellulases identified in secretomes with the highest activity.

Protein IDs	Intensity 1.5_4	Intensity 1.5_17	Intensity 2_5	Intensity pB6	PSM 1.5_4	PSM 1.5_17	PSM 2_5	PSM pB6
A_GH5	2.E+08	6.E+06	3.E+06	1.E+06	6	0	0	0
A_GH9	3.E+06	0.E+00	9.E+05	5.E+06	1	0	0	2
B_GH12	2.E+10	5.E+08	1.E+10	1.E+10	42	9	88	73
B_GH9	4.E+10	4.E+08	6.E+09	1.E+10	146	13	60	91

D. Activity Assay

The dinitrosalicylic acid (DNS) assay (7) was performed in duplicate for each secretome by reacting them with 500 μg of neutralized, phosphoric acid swollen cellulose (PASO; amorphous cellulose, FIG. **7**), 500 μg of filter paper (FP; crystalline cellulose, FIG. **8**), or 500 μg of lichenan (β-1,4- and β-1,3-linked glucan, FIG. **9**) in thin-walled strip tubes with 50 μL reaction volume. Each tube contained 20 μL of secretome protein, 25 μL of 20 mg/mL substrate solution

(prepared in water with 0.05% sodium azide, and 5 μL of 10 mM MES, pH 6. Secretome- and substrate-alone samples were included as controls. Tubes were incubated at 42° C. for 21 h for PASO and filter paper reactions, 4.5 h for lichenan reactions).

Tubes were centrifuged at 2500×g for 5 min and 30 μl of the supernatant was transferred to thin-walled PCR plates, combined with 60 μL of DNS reagent (3,5-dinitrosalicylic acid), and heated to 95° C. for 5 min. Glucose stock solutions at concentrations ranging from 0.5 to 1.5 mg/mL were included in the plate for generating a reducing sugar standard curve. 25 μL of the reactions or standards were combined with 125 μL of water in a U-bottom polystyrene 96-well plate and the absorbance was measured at 540 nm. Absorbance intensity is directly proportional to the amount of reducing sugar present and is proportional to cellulase activity. Activity was determined as the percentage of reducing sugar generated from 500 μg of polysaccharide substrate. Values were normalized to the activity present in 10 μg of total protein. The in vivo strain activity in the filter paper assay (described in Section 3) was compared to the in vitro secretome activity on PASO in FIG. **10**.

E. Results of Activity Assay

Results of the activity assay are disclosed in FIGS. **7-11**. FIG. **7** is a diagram of the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on amorphous cellulose (PASO). EV is an empty vector control containing pSET152 plasmid without cellulase genes. pACTE contains 5 ActE cellulase genes, pActE-B contains 5 ActE cellulases plus the B6 GH12 cellulase, pB6 contains 5 DpondAA-B6 cellulases, and p95 contains 6 LaPpAH-95 cellulases. From these results, we learned that at least two strains exhibited cellulase activity at least two fold higher on PASO than the best performing, non-combinatorial control operon, pB6.

FIG. **8** discloses the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on crystalline cellulose (filter paper). Samples are as described in FIG. **7**. From these results, two strains exhibited cellulase activity at least two-fold higher on filter paper than the best performing, non-recombined control operon, pB6.

Similarly, FIG. **9** discloses the activity of secretomes from *S. lividans* harboring combinatorial or control cellulolytic operons on lichenan, another cellulose source. Samples are as described in FIG. **7**. From these results, three strains exhibited glucanase activity significantly higher on lichenan (a polysaccharide consisting of alternating beta-1,3-glucan and beta-1,4-glucan linkages) than the best performing, non-recombined control operon, pB6.

FIG. **10** is a plot of the correlation between the days required for strains to break filter paper in vivo and in vitro cellulase activity of secretomes of *S. lividans* containing combinatorial (blue) or control cellulolytic operons (red). This figure is correlating the in vivo activity of the strain using filter paper as a sole carbon source with the in vitro activity of the actual secreted protein on cellulose. The latter result is a direct measure of the secreted products of the cassette plus other secreted *lividans* proteins. This correlation is of interest as it shows the relationship between strain metabolic activity and actual secreted protein and can help indicate the best route toward commercial success of the invention. One application of the modified strains could be to use the living engineered strain for biomass digestion and another application could be to harvest the secreted proteins generated from the strain.

5. Genomic Data

Spores from 10 exceptional strains were added to 5 mL of SGGP (0.4% tryptone, 0.4% yeast extract, 0.05% $MgSO_4$, 1% glucose. 0.2% glycine, 0.01 M potassium phosphate buffer, pH 7.0) medium with 50 μg/mL apramycin, and genomic DNA was purified according to page 162 of (8). DNA samples were submitted to the University of Wisconsin Biotechnology Center for library preparation and sequencing. Sequencing was performed via Illumina MiSeq with a paired-end 220-bp read length. Both raw reads and Bowtie 2 (9) assemblies were examined for matches to genes from the combinatorial library.

FIG. **11** is a diagram disclosing the presence of genes assigned from direct Illumina sequencing of *S. lividans* harboring combinatorial cellulolytic operons. The combination of GH9 from 95 and GH12 from B6 (isolate 2-5) is a preferred combination because of the increased cellulolytic activity of this isolate. Combinations of GH9 (from B6), GH12 (from B6), and GH5 (from ActE) are also preferred.

FIG. **12** is a diagram containing examples of combinatorial gene operons produced for the Example 2 experiments. Each strain may contain a GH6, LPMO, GH48, GH5, GH9, and GH12 derived from any of the three host cellulolytic *Streptomyces* strains as depicted. Optimal cellulolytic operon combinations are selected by the engineered strain's ability to break filter paper faster than wild-type host strains and/or strains expressing the non-combinatorial operons described in FIG. **3**.

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SEQUENCE LISTING

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Ser Ala Asp Ala Ala Arg Ala Ala Ala Ala Gly Ser Gly Tyr Trp His
        35                  40                  45

Thr Ser Gly Arg Gln Ile Leu Asp Ala Ala Asn Gln Pro Val Arg Ile
    50                  55                  60

Ala Gly Ile Asn Trp Phe Gly Phe Glu Thr Ala Asn Tyr Val Pro His
65                  70                  75                  80

Gly Leu Trp Ser Arg Asp Tyr Lys Ser Met Ile Asp Gln Met Arg Ser
                85                  90                  95

Leu Gly Tyr Asn Thr Ile Arg Leu Pro Tyr Ser Asp Asp Ile Phe Ala
            100                 105                 110

Gly Thr Glu Pro Ala Ser Ile Asn Tyr Ser Ala Gly Met Asn Thr Asp
        115                 120                 125

Leu Ala Gly Leu Asn Ser Leu Gln Val Met Asp Arg Ile Val Asp His
    130                 135                 140

Ala Gly Ser Phe Gly Met Lys Val Ile Leu Asp Arg His Arg Pro Asp
145                 150                 155                 160

Ser Ala Gly Gln Ser Ala Leu Trp Tyr Thr Ser Ala Val Pro Glu Ser
                165                 170                 175

Thr Trp Leu Ala His Leu Lys Ser Leu Ala Ala Arg Tyr Ala Gly Asn
            180                 185                 190

Asp Ala Val Val Gly Ile Asp Leu His Asn Glu Pro His Asp Pro Ala
        195                 200                 205

Cys Trp Gly Cys Gly Asp Thr Thr Lys Asp Trp Arg Leu Ala Ala Gln
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Arg Gly Gly Asn Ala Ala Leu Ser Ala Asn Pro Asp Leu Leu Ile Phe
225                 230                 235                 240

Val Glu Gly Val Gln Thr Val Asp Gly Val Ser Gly Trp Trp Gly Gly
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-continued

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            260                 265                 270

Lys Val Val Tyr Ser Ala His Asp Tyr Ala Thr Ser Val Ala Gln Gln
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Pro Trp Phe Thr Asp Ser Ser Phe Pro Asp Asn Met Pro Gly Val Trp
    290                 295                 300

Asp Lys Tyr Trp Gly Tyr Ile Phe Lys Gln Asn Ile Ala Pro Val Trp
305                 310                 315                 320

Val Gly Glu Phe Gly Thr Thr Leu Gln Ser Thr Thr Asp Gln Lys Trp
                325                 330                 335

Leu Lys Ala Leu Ala Asp Tyr Leu Arg Pro Thr Ser Gln Tyr Gly Ala
            340                 345                 350

Asp Ser Phe Ser Trp Thr Phe Trp Ser Trp Asn Pro Asn Ser Gly Asp
        355                 360                 365

Thr Gly Gly Ile Leu Lys Asp Asp Trp Thr Ser Val Asp Thr Val Lys
    370                 375                 380

Asp Gly Tyr Leu Ala Ser Ile Lys Ala Pro Asp Phe Gly Asn Gly Gly
385                 390                 395                 400

Gly Ser Gly Gly Asp Asp Asp Thr Gln Ala Pro Thr Ala Pro Thr Gly
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Gly Ser Gly Gly Asn Thr Gly Cys Lys Ala Val Tyr Thr Val Asn Gly
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Thr Ala Pro Ala Thr Ser Trp Lys Leu Thr Trp Thr Tyr Gly Gly Ser
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Gln Lys Ile Thr Asn Met Trp Asn Ala Ser Tyr Thr Gln Ser Gly Ala
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Ser Val Thr Val Thr Ser Thr Asp Tyr Asn Gly Gly Leu Ala Ala Gly
                565                 570                 575

Ala His Thr Gly Phe Gly Phe Gln Gly Thr Pro Ala Ala Gly Ala Val
            580                 585                 590

Pro Thr Val Ser Cys Thr Leu Ser
        595                 600


<210> SEQ ID NO 2
<211> LENGTH: 1761
<212> TYPE: DNA
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 2

atgagtcgta cgtcccgcac cacactgcgt cgcagtcgga cggcgctgat ggcagcaggt     60

gcactcgtcg cggcagccgc agggagcgca gcagcagccg ctccgttcgg agcaacggca    120
```

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```
gcggccgcag caggatgcac ggtcgactat aagatccaga accagtggaa tggcggtctg    180

acagcatcag tctccgtgac aaacaacggg gacgccatct caggttggca gctgcagtgg    240

agcttcgcag gcggagagca ggtcagccag ggttggaatg ccacagtatc ccagagcgga    300

tcggcagtca cggccaagga cgcaggttat aacgcagcgc tcgccaccgg agcctcggcc    360

agcttcggtt tcaatgcaac gggcaatgga aacagcgtcg ttccggcaac cttcaagttg    420

aatggtgtaa cctgcaacgg gggtacgaca ggaccgacgg acccgacaga cccgaccgac    480

cccaccgacc cgacagaccc cccggcaggt aatcgagtgg acaaccctta ccagggagca    540

aaggtttatg tcaacccgga atggtccgcc aacgccgcag ccgaacccgg cggtgaccgc    600

atagcggacc agccgacagg tgtctggttg gatcgtatag cggccatcga gggggccaat    660

ggaagtatgg gccttcgcga ccacctggac gaagcgttga cgcaaaaagg aagcggagag    720

ctggtggtcc aagtggtcat ctacaatctc ccaggtcgtg actgtgccgc actggcctcg    780

aacggagaac tcgggccgac cgagatcgga cgctacaaaa cagaatatat cgatccgata    840

gcggagatcc tgggtgaccc gaagtacgca gggctccgga tcgtgacgac ggtagaaatc    900

gatagtctgc cgaatttggt cactaatgcc ggaggacgtc caacggcaac accggcgtgc    960

gacgtcatga aagccaacgg taattatgtg aagggtgtcg gatatgcact gaacaagctc   1020

ggggatgcgc cgaatgtgta caattatatc gacgcaggcc atcacggatg gatcggatgg   1080

gatgacaact tcggcgcctc tgcagagatc ttccacgaag cggccaccgc agaggggcca   1140

acggtcaacg acgtccatgg tttcatcacc aacacagcga actactcagc gctgaaggaa   1200

gagaacttct cgatcgatga tgcagtaaac ggcaccagcg tccgccagtc taagtgggtg   1260

gactggaatc gatacacaga cgagctcagc ttcgcccagg cattccgcaa tgaactcgtg   1320

agtgtgggtt tcaactccgg tatcggaatg ctgattgaca cgtcgcggaa cggttggggc   1380

ggagcaaatc gtccgtcggg cccgggtgcc aatacatccg tcgacacgta tgtagacgga   1440

ggccgctacg atcgacggat ccatctcggt aactggtgta atcaggcagg tgcgggactc   1500

ggtgaacgcc cgcaggctgc gccagaaccg ggcatcgacg cctacgtgtg gatgaagccc   1560

ccgggagaga gtgacggatc cagctccgaa attccgaacg atgagggcaa gggattcgac   1620

cgtatgtgcg acccgacata cacgggcaac gcacggaata acaacaatat gagtggcgcg   1680

ctgggaggtg cccccgtctc gggaaagtgg ttcagtgccc aattccaaga gctgatgaaa   1740

aatgcgtatc cggcattgtg a                                             1761
```

<210> SEQ ID NO 3
<211> LENGTH: 710
<212> TYPE: PRT
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 3

```
Met Ser Thr Arg Gly Thr Ile Lys Gln Gly Leu Arg Arg Arg Leu Ala
1               5                   10                  15

Ala Ala Ser Ala Leu Ala Met Gly Ala Ala Leu Ala Val Ala Ile Pro
            20                  25                  30

Thr Thr Ala Asp Ala Ala Ala Ala Arg Val Asp Asn Pro Tyr Val Gly
        35                  40                  45

Ala Lys Ala Tyr Val Asn Pro Asp Trp Ser Ala Lys Ala Ala Ala Glu
    50                  55                  60

Pro Gly Gly Ala Ala Ile Ala Asp Thr Pro Ala Phe Val Trp Met Asp
65                  70                  75                  80
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```
Arg Ile Ala Ala Ile Gly Gly Thr Pro Gly Ala Met Ser Leu Arg Glu
                85                  90                  95

His Leu Asp Thr Ala Leu Asp Gln Gly Ala Asn Leu Phe Gln Val Val
            100                 105                 110

Ile Tyr Asp Leu Pro Gly Arg Asp Cys Ala Ala Leu Ala Ser Asn Gly
        115                 120                 125

Glu Leu Gly Pro Thr Glu Leu Asp Arg Tyr Lys Ser Glu Tyr Ile Asp
    130                 135                 140

Pro Ile Ser Glu Ile Leu Ala Asp Pro Ala Tyr Ala Asn Leu Arg Ile
145                 150                 155                 160

Val Thr Ile Ile Glu Pro Asp Ser Leu Pro Asn Ile Val Thr Asn Ala
                165                 170                 175

Gly Gly Thr Ala Gly Ser Thr Asp Ala Cys Ala Thr Met Lys Ala Asn
            180                 185                 190

Gly Asn Tyr Glu Lys Gly Val Gly Tyr Ala Leu His Thr Leu Gly Ala
        195                 200                 205

Ile Pro Asn Val Tyr Asn Tyr Val Asp Ala Ala His His Gly Trp Leu
    210                 215                 220

Gly Trp Asp Ser Asn Met Val Pro Ala Gly Val Glu Phe Lys Lys Ala
225                 230                 235                 240

Ala Thr Ser Glu Gly Ala Thr Val Asp Asp Val Ala Gly Phe Ile Val
                245                 250                 255

Asn Thr Ala Asn Tyr Ser Ala Leu Lys Glu Pro Asn Phe Lys Ile Thr
            260                 265                 270

Asp Ser Val Asn Gly Thr Thr Val Arg Gln Ser Lys Trp Val Asp Trp
        275                 280                 285

Asn Tyr Tyr Thr Asp Glu Leu Ser Phe Ala Gln Ala Leu Arg Thr Gln
    290                 295                 300

Leu Val Gly Gln Gly Phe Asn Ser Asn Ile Gly Met Leu Ile Asp Thr
305                 310                 315                 320

Ala Arg Asn Gly Trp Gly Gly Ser Asp Arg Pro Thr Ser Ala Gly Pro
                325                 330                 335

Leu Thr Ser Val Asp Asp Tyr Val Asn Gly Gly Arg Val Asp Arg Arg
            340                 345                 350

Ile His Ala Gly Asn Trp Cys Asn Gln Ser Gly Ala Gly Ile Gly Glu
        355                 360                 365

Arg Pro Thr Ser Ala Pro Glu Ala Gly Ile Asp Ala Tyr Val Trp Ala
    370                 375                 380

Lys Pro Pro Gly Glu Ser Asp Gly Ser Ser Gln Ala Glu Asp Asn Asp
385                 390                 395                 400

Glu Gly Lys Gly Phe Asp Arg Met Cys Asp Pro Thr Tyr Glu Gly Asn
                405                 410                 415

Gly Arg Asn Gly Asn Ser Lys Thr Gly Ala Leu Pro Asn Ser Pro Val
            420                 425                 430

Ala Gly His Trp Phe Ser Ala Gln Phe Gln Glu Leu Val Arg Asn Ala
        435                 440                 445

Tyr Pro Pro Ile Asp Gly Ser Gly Glu Asn Pro Gly Gly Gly Gly Asp
    450                 455                 460

Asp Asp Thr Gln Ala Pro Thr Ala Pro Thr Gly Leu Thr Ser Ser Ala
465                 470                 475                 480

Lys Thr Ser Ser Ser Val Ser Leu Ser Trp Thr Ala Ser Ser Asp Asn
                485                 490                 495
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```
Lys Ala Val Thr Gly Tyr Asp Val Tyr Arg Gly Gly Thr Lys Val Gly
            500                 505                 510

Ser Thr Thr Thr Thr Ser Tyr Thr Asp Thr Gly Leu Ser Ala Ser Thr
        515                 520                 525

Ala Tyr Ser Tyr Thr Val Lys Ala Lys Asp Ala Ala Gly Asn Val Ser
    530                 535                 540

Ala Ala Ser Ser Ala Leu Ser Val Thr Thr Ser Ala Gly Gly Gly Thr
545                 550                 555                 560

Gly Thr Gly Ser Leu Lys Val Gln Tyr Lys Asn Asn Asp Asn Ser Pro
                565                 570                 575

Thr Asp Asn Gln Ile Arg Phe Gly Leu Gln Leu Val Asn Thr Gly Ser
            580                 585                 590

Ser Ala Val Asp Leu Ser Thr Val Lys Leu Arg Tyr Trp Phe Thr Pro
        595                 600                 605

Glu Ser Gly Ser Ser Thr Phe Gly Thr Ala Cys Asp Tyr Ala Val Leu
    610                 615                 620

Gly Cys Gly Lys Leu Ser Leu Ala Val Gln Ser Gly Gly Ser Ala Ala
625                 630                 635                 640

Gly Ala Ser His Tyr Leu Glu Val Ser Phe Gly Ser Gly Ser Leu Ala
                645                 650                 655

Ala Gly Ala Ser Thr Gly Glu Met Gln Leu Arg Leu Asn Lys Ser Asp
            660                 665                 670

Trp Ser Asn Phe Asn Glu Ala Asp Asp Tyr Ser His Gly Thr Gly Thr
        675                 680                 685

Ser Phe Ala Asp Ala Ser Lys Ile Gly Val Tyr Thr Ala Gly Ala Leu
    690                 695                 700

Ser Trp Gly Thr Ala Pro
705                 710


<210> SEQ ID NO 4
<211> LENGTH: 790
<212> TYPE: PRT
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 4

Met Arg Ser Phe Pro Leu Pro Ala Leu Arg Arg Arg Ser Arg Arg Pro
1               5                   10                  15

Gly Arg Pro Leu Gly Ala Val Ala Leu Ala Leu Ala Val Gly Ala Gly
            20                  25                  30

Leu Leu Leu Pro Leu Ser Leu Pro Ala Gly Ala Ala Ala Ala Pro Ala
        35                  40                  45

Phe Asp Tyr Gly Glu Ala Leu Gln Lys Ser Val Leu Phe Tyr Glu Ala
    50                  55                  60

Gln Gln Ser Gly Lys Leu Pro Asp Thr Asn Arg Val Ser Trp Arg Gly
65                  70                  75                  80

Asp Ser Ala Leu Asp Asp Gly Lys Asp Ala Gly Leu Asp Leu Thr Gly
                85                  90                  95

Gly Trp Tyr Asp Ala Gly Asp His Val Lys Phe Gly Leu Pro Met Ala
            100                 105                 110

Tyr Ser Ala Thr Met Leu Ala Trp Gly Gly Thr Glu Gln Arg Ala Ala
        115                 120                 125

Tyr Glu Ala Ser Gly Gln Leu Pro His Leu Arg Asn Asn Leu Arg Phe
    130                 135                 140

Val Asp Asp Tyr Leu Leu Lys Ala His Pro Ser Pro Asn Val Leu Tyr
145                 150                 155                 160
```

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```
Gly Gln Val Gly Asn Gly Gly Asp Asp His Lys Trp Trp Gly Pro Ala
                165                 170                 175

Glu Val Met Pro Met Lys Arg Pro Ala Tyr Lys Ile Asp Ala Ser Cys
            180                 185                 190

Pro Gly Ser Asp Leu Ala Gly Gln Thr Ala Ala Ala Leu Ala Ser Ser
        195                 200                 205

Ser Met Val Phe Ser Asp Ser Asp Pro Ala Tyr Ala Ala Lys Leu Ile
    210                 215                 220

Thr His Ala Lys Gln Leu Tyr Thr Phe Ala Asp Thr Tyr Arg Gly Lys
225                 230                 235                 240

Tyr Ser Asp Cys Ile Thr Asp Ala Gln Ser Tyr Tyr Asn Ser Trp Ser
                245                 250                 255

Gly Tyr Asn Asp Glu Leu Val Trp Gly Ala Ile Trp Leu Tyr Lys Ala
            260                 265                 270

Thr Gly Asp Thr Ala Tyr Leu Ala Lys Ala Glu Ser Tyr Tyr Asp Asn
        275                 280                 285

Leu Ser Thr Glu Pro Gln Thr Thr Thr Arg Ser Tyr Arg Trp Thr Leu
    290                 295                 300

Ser Trp Asp Asp Thr Ser Tyr Gly Ala Tyr Val Leu Leu Ala Gln Leu
305                 310                 315                 320

Thr Gly Lys Gln Lys Tyr Ile Asp Asp Ala Asn Arg Trp Leu Asp Trp
                325                 330                 335

Trp Thr Val Gly Val Asn Gly Gln Arg Val Pro Tyr Ser Pro Gly Gly
            340                 345                 350

Gln Ala Val Leu Asp Ser Trp Gly Ser Leu Arg Tyr Ala Ala Asn Thr
        355                 360                 365

Ala Phe Val Ala Leu Ser Tyr Ser Asp Trp Leu Thr Gly Asp Ala Thr
    370                 375                 380

Arg Lys Ala Arg Tyr His Asp Phe Ala Val Arg Gln Ile Asp Tyr Ala
385                 390                 395                 400

Leu Gly Asp Asn Pro Arg Gly Ser Ser Tyr Val Val Gly Phe Gly Glu
                405                 410                 415

Asn Pro Pro Thr Lys Pro His His Arg Thr Ala His Gly Ser Trp Thr
            420                 425                 430

Asp Gln Met Thr Asn Pro Val Glu Thr Arg His Thr Leu Tyr Gly Ala
        435                 440                 445

Leu Val Gly Gly Pro Ser Ala Pro Asp Asp Thr Tyr Thr Asp Asp Arg
    450                 455                 460

Gly Asn Tyr Val Asn Asn Glu Val Ala Thr Asp Tyr Asn Ala Ala Phe
465                 470                 475                 480

Thr Gly Ala Leu Ala Arg Leu Tyr Ala Glu Tyr Gly Gly Ser Pro Leu
                485                 490                 495

Thr Asp Phe Pro Gln Pro Glu Glu Pro Asp Gly Pro Glu Met Ser Val
            500                 505                 510

Gln Ala Ser Val Asn Ala Ala Gly Ala Asn Phe Thr Glu Val Lys Ala
        515                 520                 525

Tyr Leu Ile Asn Arg Ser Ala Trp Pro Ala Arg Ala Leu Thr Asp Ala
    530                 535                 540

Ser Val Arg Tyr Tyr Phe Thr Leu Glu Pro Gly Val Ala Pro Gly Asp
545                 550                 555                 560

Ile Ser Phe Thr Thr Asn Tyr Asn Gln Cys Gly Glu Val Thr Gly Pro
                565                 570                 575
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```
Thr His Leu Thr Gly Asp Val Tyr Tyr Ala Thr Val Asp Cys Ser Asp
            580                 585                 590

Thr Asp Ile Ala Pro Ala Gly Gln Ser Ala Tyr Arg Lys Glu Val Gln
        595                 600                 605

Phe Arg Ile Ser Ser Ala Gly Ala Trp Asp Pro Ser Asn Asp Trp Ser
    610                 615                 620

Tyr Pro Ser Thr Ala Thr Thr Pro Gly Gly Thr Pro Val Asp Ala Pro
625                 630                 635                 640

His Met Val Leu Leu Glu Gly Ser Ala Pro Gln Trp Gly Thr Ala Pro
                645                 650                 655

Asp Gly Thr Asp Pro Gly Pro Gly Pro Asp Pro Thr Thr Thr Pro Glu
            660                 665                 670

Pro Ser Pro Thr Pro Asp Pro Thr Asp Thr Pro Asp Pro Glu Pro Gly
        675                 680                 685

Ala Cys Asp Val Thr Tyr Arg Val Ser Gln Ala Trp Gly Thr Gly Phe
    690                 695                 700

Thr Ala Asp Val Thr Val Lys Asn Thr Gly Pro Thr Pro Leu Asp Gly
705                 710                 715                 720

Trp Gln Leu Ala Phe Asp Phe Gln Gly Ala Glu Ser Val Ser Asn Ala
                725                 730                 735

Trp Asn Ala Thr Ala Thr Gln Ser Gly Thr Arg Val Thr Leu Lys Asn
            740                 745                 750

Ala Gly His Asn Gly Ser Val Pro Ala Gly Gly Ser Ala Ser Phe Gly
        755                 760                 765

Phe Gln Ala Asn Gly Ala Pro Gly Ala Asp Pro His Ser Phe Thr Leu
    770                 775                 780

Asn Gly Lys Glu Cys Gly
785                 790


<210> SEQ ID NO 5
<211> LENGTH: 428
<212> TYPE: PRT
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 5

Met Thr Gly Arg Pro Leu Pro Ala Leu Ala Gly Ala Ala Ala Ala Leu
1               5                   10                  15

Val Leu Ala Ala Ala Ser Met Leu Thr Gly Ala Ser Ser Ala Ser Ala
            20                  25                  30

Ser Pro Val Thr Asp Cys Thr Pro Trp Gly Thr Thr Glu Leu Leu Gly
        35                  40                  45

Gly Glu Tyr Leu Tyr Gln Gln Asn Glu Trp Asn Ser Asp Ser Glu Gln
    50                  55                  60

Cys Val Gly Val Asp Pro Asp Thr Gly Ala Trp Ser Val Thr Thr Ser
65                  70                  75                  80

Ser Phe Asn Leu Pro Thr Asn Gly Ala Pro Ala Thr Tyr Pro Ser Ser
                85                  90                  95

Tyr Lys Gly Cys His Trp Gly Ala Cys Thr Ser Asp Ser Gly Leu Pro
            100                 105                 110

Leu Arg Val Asp Glu Leu Gly Ser Val His Thr Asp Trp Ser Thr Thr
        115                 120                 125

Gln Val Gly Ser Gly Ala Tyr Asn Val Ser Met Asp Val Trp Phe Asn
    130                 135                 140

Ser Ala Pro Val Thr Asp Asp Gln Pro Asp Gly Thr Glu Leu Met Ile
145                 150                 155                 160
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```
Trp Met Asn His Arg Gly Gly Val Gln Pro Ile Gly Ser Arg Thr Ala
                165                 170                 175

Thr Val Gln Leu Asp Gly Arg Thr Trp Asp Val Trp Thr Gly Pro Gly
            180                 185                 190

Ala Ser Gly Trp Lys Val Ile Ser Tyr Val Leu Gln Gly Gly Ala Thr
        195                 200                 205

Glu Leu Thr Gly Phe Asp Val Lys Ser Leu Ile Asp Asp Gly Val Gly
    210                 215                 220

Arg Gly Gln Ile Asp Pro Ala His Tyr Leu Ile Asp Ala Glu Ala Gly
225                 230                 235                 240

Phe Glu Ile Trp Gln Gly Gly Gln Gly Leu Gly Met Lys Glu Phe Ser
                245                 250                 255

Phe Glu Ala Ser Ala Gly Thr Asp Gly Gly Asp Asp Gly Gly Asp Gly
            260                 265                 270

Asp Pro Gly Gly Gly Gly Thr Thr Gly Ala Leu Lys Ala Gln Tyr Lys
        275                 280                 285

Asn Asn Asp Ser Ser Ala Thr Asp Asn Gln Ile Arg Pro Gly Leu Gln
    290                 295                 300

Leu Val Asn Thr Gly Ser Thr Ala Val Asp Leu Ser Thr Val Lys Leu
305                 310                 315                 320

Arg Tyr Trp Phe Thr Pro Glu Ser Gly Ala Ala Gly Phe Gly Thr Ala
                325                 330                 335

Cys Asp Tyr Ala Val Val Gly Cys Gly Asn Val Thr His Thr Val Lys
            340                 345                 350

Gln Ala Gly Thr Ala Ala Gly Ala Ser His Tyr Leu Glu Val Gly Phe
        355                 360                 365

Thr Gly Gly Ser Leu Ala Pro Gly Ala Ser Thr Gly Glu Ile Gln Leu
    370                 375                 380

Arg Phe Asn Lys Ser Asp Trp Ser Ala Phe Asp Glu Ala Asp Asp Tyr
385                 390                 395                 400

Ser Arg Ala Ala Asn Thr Ala Phe Thr Asp Ala Ser Lys Val Gly Val
                405                 410                 415

Tyr Val Asn Gly Ala Leu Ser Ser Gly Thr Ala Pro
            420                 425


<210> SEQ ID NO 6
<211> LENGTH: 920
<212> TYPE: PRT
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 6

Met Leu Ala Val Gly Leu Ala Gln Gly Thr Ala Ile Ala Arg Pro Ala
1               5                   10                  15

Ser Ala Gln Ala Gly Thr Gly Ala Arg Ala Ala Ala Ala Gly Asp Asp
            20                  25                  30

Pro Tyr Thr Gln Ala Phe Leu Thr Gln Tyr Gly Lys Leu Lys Asp Ala
        35                  40                  45

Ala Asn Gly Tyr Phe Ser Pro Asp Gly Leu Pro Tyr His Ser Val Glu
    50                  55                  60

Thr Leu Met Val Glu Ala Pro Asp His Gly His Gln Thr Thr Ser Glu
65                  70                  75                  80

Ala Val Ser Phe Trp Met Trp Leu Glu Ala Ala Tyr Gly Arg Val Thr
                85                  90                  95

Gly Asp Trp Ala Pro Phe Asn Ala Ala Trp Ala Val Ala Glu Lys Thr
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           100                 105                 110

Ile Ile Pro Gln His Ala Asp Gln Ser Thr Ser Asp Ser Tyr Asn Pro
        115                 120                 125

Ser Ala Pro Ala Thr Tyr Ala Pro Glu His Pro Leu Pro Ser Gly Tyr
    130                 135                 140

Pro Ser Ala Leu Asp Gly Thr Val Pro Val Gly Thr Asp Pro Leu Ser
145                 150                 155                 160

Ala Glu Leu Ala Ser Ser Tyr Gly Thr Met Asp Val Tyr Gly Met His
                165                 170                 175

Trp Leu Met Asp Leu Asp Asn Val Tyr Gly Tyr Gly Asn Lys Pro Gly
            180                 185                 190

Thr Gly Gly Glu Ser Gly Pro Gly Ala Gly Ala Ser Phe Ile Asn Thr
        195                 200                 205

Tyr Gln Arg Gly Ala Gln Glu Ser Val Trp Glu Thr Val Pro Gln Pro
    210                 215                 220

Thr Thr Asp Leu Phe Lys Tyr Gly Gly Pro Asn Gly Tyr Leu Asp Leu
225                 230                 235                 240

Phe Val Gly Asp Ser Ser Tyr Ala Lys Gln Trp Lys Tyr Thr Asn Ala
                245                 250                 255

Pro Asp Ala Asp Ala Arg Ala Val Gln Ala Ala Tyr Trp Ala Tyr Arg
            260                 265                 270

Trp Ala Ser Glu Gln Gly Lys Glu Ser Gln Val Ala Ala Ser Val Ala
        275                 280                 285

Lys Ala Ala Lys Met Gly Asp Tyr Leu Arg Tyr Ala Met Phe Asp Lys
    290                 295                 300

Tyr Phe Lys Arg Val Gly Asp Cys Thr Asp Pro Asn Ser Cys Pro Ala
305                 310                 315                 320

Ala Ser Gly Arg Asp Ser Gln His Tyr Leu Leu Ser Trp Tyr Tyr Ala
                325                 330                 335

Trp Gly Gly Ala Ala Ala Gly Ser Gly Gly Gly Trp Ala Trp Arg Ile
            340                 345                 350

Gly Asp Gly Ala Ser His Gln Gly Tyr Gln Asn Pro Leu Ala Ala Trp
        355                 360                 365

Ala Leu Ser Asn Val Pro Ser Leu Thr Pro Lys Ser Ala Thr Ala Arg
    370                 375                 380

Ser Asp Trp Ser Lys Ser Leu Thr Arg Gln Leu Glu Phe Leu Thr Trp
385                 390                 395                 400

Leu Gln Ser Ser Glu Gly Ala Leu Ala Gly Gly Cys Thr Asn Ser Trp
                405                 410                 415

Glu Gly Ser Tyr Ser Thr Pro Pro Ala Gly Thr Pro Thr Phe Tyr Gly
            420                 425                 430

Met Ala Tyr Asp Trp Gln Pro Val Tyr His Asp Pro Ala Ser Asn Asn
        435                 440                 445

Trp Phe Gly Phe Gln Ala Trp Gly Met Glu Arg Val Ala Ala Tyr Tyr
    450                 455                 460

Tyr Val Thr Gly Asn Ala Thr Ala Glu Ala Val Leu Ser Lys Trp Val
465                 470                 475                 480

Ala Trp Ala Ser Ser Glu Thr Thr Ile Gly Ser Asp Gly Ser Phe Arg
                485                 490                 495

Phe Pro Ser Thr Leu Asn Trp Thr Gly Glu Pro Asp Thr Trp Asn Ala
            500                 505                 510

Ala Ser Pro Gly Asp Asn Ala Gly Leu His Val Ser Val Val Asp Tyr
        515                 520                 525
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```
Ala Asn Asp Val Gly Val Gly Ala Ala Tyr Val Lys Thr Leu Thr Tyr
    530                 535                 540

Tyr Ala Ala Lys Ser Gly Asp Glu Asp Ala Ala Ala Leu Ala Lys Ala
545                 550                 555                 560

Leu Leu Asp Ala Met Ala Leu Asn Thr Thr Asp Lys Gly Ile Ser Val
                565                 570                 575

Pro Glu Thr Arg Leu Asp Tyr Asn Arg Phe Asp Asp Glu Val Tyr Ile
            580                 585                 590

Pro Ser Gly Trp Ser Gly Thr Met Pro Asn Gly Asp Pro Val Arg Pro
        595                 600                 605

Gly Ser Thr Phe Ile Ser Ile Arg Ser Trp Tyr Lys Asp Asp Pro Asp
    610                 615                 620

Trp Pro Lys Val Gln Ala Tyr Leu Asp Gly Gly Asp Ala Pro Val Phe
625                 630                 635                 640

Thr Tyr His Arg Phe Trp Ala Gln Ala Ala Leu Ala Leu Ala Phe Ala
                645                 650                 655

Ile Tyr Ala Glu Leu Leu Val Glu Gly Gly Gly Gly Glu Pro Gly Gly
            660                 665                 670

Asp Thr Glu Pro Pro Thr Ala Pro Gly Gly Leu Thr Val Thr Ala Thr
        675                 680                 685

Thr Lys Asp Ser Val Ser Leu Ser Trp Ser Ala Ser Thr Asp Asn Thr
    690                 695                 700

Ala Val Thr Gly Tyr Asp Val Tyr Arg Asn Gly Val Leu Ala Gly Asn
705                 710                 715                 720

Ala Thr Gly Arg Thr Phe Thr Asp Ser Gly Leu Ala Ala Asn Thr Glu
                725                 730                 735

Tyr Thr Tyr Ala Val Ala Ala Arg Asp Ala Gly Gly Asn Thr Ser Ala
            740                 745                 750

Leu Ser Asp Ala Val Leu Ala Lys Thr Lys Thr Gly Gly Ser Thr Gly
        755                 760                 765

Thr Gly Ala Val Lys Val Gln Tyr Lys Ser Thr Asp Ser Ser Ala Thr
    770                 775                 780

Asp Asn Gln Ile Arg Met Gly Leu Gln Val Val Asn Thr Gly Ser Ala
785                 790                 795                 800

Pro Val Asp Leu Ser Thr Val Lys Val Arg Tyr Trp Phe Thr Ala Asp
                805                 810                 815

Gly Gly Pro Ser Thr Phe Gly Thr Tyr Cys Asp Tyr Ala Ala Leu Gly
            820                 825                 830

Ser Ser Thr Ile Thr His Thr Val Val Ala Val Ser Ser Pro Lys Thr
        835                 840                 845

Gly Ala Asp Arg Tyr Leu Glu Val Gly Phe Thr Gly Gly Ala Gly Thr
    850                 855                 860

Leu Ala Ala Gly Ala Ser Thr Gly Glu Ile Gln Leu Arg Leu Asn Lys
865                 870                 875                 880

Ser Asp Trp Ser Asn Phe Asn Glu Ala Asp Asp Tyr Ser Arg Ala Thr
                885                 890                 895

Asn Thr Ala Tyr Ala Asp Ser Ser Lys Val Gly Ala Tyr Val Ala Gly
            900                 905                 910

Ala Leu Ala Trp Gly Val Glu Pro
        915                 920
```

<210> SEQ ID NO 7
<211> LENGTH: 367

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<212> TYPE: PRT
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 7

Met Ala Arg Arg Arg Thr Gln Leu Ala Ser Leu Ala Ala Val Leu Ala
1 5 10 15

Thr Leu Leu Gly Gly Ile Ala Phe Thr Leu Leu Gly Gln Gly Ser Ala
20 25 30

Gln Ala His Gly Val Thr Met Ser Pro Gly Ser Arg Thr Tyr Leu Cys
35 40 45

Trp Leu Asp Ala Lys Thr Ser Thr Gly Ser Leu Asp Pro Thr Asn Pro
50 55 60

Ala Cys Lys Ala Ala Leu Ala Glu Ser Gly Ala Ser Ser Leu Tyr Asn
65 70 75 80

Trp Phe Ala Val Leu Asp Ser Asn Ala Gly Gly Arg Gly Ala Gly Tyr
85 90 95

Val Pro Asp Gly Thr Leu Cys Ser Ala Gly Asp Arg Ser Pro Tyr Asn
100 105 110

Phe Thr Gly Tyr Asn Ala Ala Arg Gly Asp Trp Pro Arg Thr His Leu
115 120 125

Thr Ser Gly Ala Lys Ile Glu Val Asp His Ser Asn Trp Ala Ala His
130 135 140

Pro Gly Glu Phe Arg Val Tyr Met Ser Lys Pro Gly Tyr Ser Pro Thr
145 150 155 160

Thr Glu Leu Gly Trp Asp Asp Leu Asp Leu Ile Gln Thr Val Ser Asn
165 170 175

Pro Pro Gln Val Gly Ser Pro Gly Thr Asp Gly Gly His Tyr Tyr Trp
180 185 190

Asp Leu Thr Leu Pro Ser Gly Arg Ser Gly Asp Ala Val Met Phe Ile
195 200 205

Gln Trp Val Arg Ser Asp Ser Gln Glu Asn Phe Phe Ser Cys Ser Asp
210 215 220

Ile Val Phe Asp Gly Gly Asn Gly Glu Val Thr Gly Ile Arg Gly Ser
225 230 235 240

Gly Ser Thr Pro Asp Pro Asp Pro Thr Asp Pro Thr Pro Asp Pro Thr
245 250 255

Asp Pro Thr Asp Pro Thr Asp Pro His Thr Gly Cys Met Ala Val Tyr
260 265 270

Asn Val Thr Asn Ser Trp Ser Gly Gly Phe Gln Gly Ser Val Glu Val
275 280 285

Met Asn His Asn Thr Thr Ala Leu Asp Gly Trp Ala Val Gln Trp Lys
290 295 300

Pro Gly Thr Gly Thr Thr Val Ser Ser Val Trp Ser Gly Val Leu Ser
305 310 315 320

Thr Gly Ser Asp Gly Thr Leu Thr Val Lys Asn Ala Asp Tyr Asn Arg
325 330 335

Ser Ile Pro Pro Asp Gly Ser Val Thr Phe Gly Phe Thr Ala Thr Ser
340 345 350

Thr Gly Asn Asp Phe Pro Val Gly Ser Ile Gly Cys Val Ser Pro
355 360 365

<210> SEQ ID NO 8
<211> LENGTH: 954
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp SirexAA-E

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<400> SEQUENCE: 8

```
Met Ala Ala Leu Ala Leu Pro Leu Gly Met Thr Ala Ala Ala Gly Thr
1               5                  10                  15

Glu Ala Gln Ala Ala Ala Val Ala Cys Ser Val Asp Tyr Thr Thr Ser
            20                  25                  30

Asp Trp Gly Ser Gly Phe Thr Thr Glu Leu Thr Leu Thr Asn Arg Gly
        35                  40                  45

Ser Ala Ala Ile Asp Gly Trp Thr Leu Thr Tyr Asp Tyr Ala Gly Asn
    50                  55                  60

Gln Gln Leu Thr Ser Gly Trp Ser Gly Thr Trp Ser Gln Ser Gly Lys
65                  70                  75                  80

Thr Val Ser Val Lys Asn Ala Ala Trp Asn Gly Ala Ile Ala Ala Gly
                85                  90                  95

Ala Ala Val Thr Thr Gly Ala Gln Phe Thr Tyr Ser Gly Ala Asn Thr
            100                 105                 110

Ala Pro Thr Thr Phe Ala Val Asn Gly Thr Val Cys Ala Gly Ala His
        115                 120                 125

Gln Pro Pro Ile Ala Val Leu Thr Ser Pro Ala Ala Gly Ala Val Phe
    130                 135                 140

Ser Ala Gly Asp Pro Val Pro Leu Ala Ala Thr Ala Ala Ala Ala Asp
145                 150                 155                 160

Gly Ala Thr Ile Ser Lys Val Glu Phe Tyr Asp Asp Thr Thr Leu Leu
                165                 170                 175

Gly Thr Asp Thr Thr Ser Pro Tyr Ser Tyr Glu Ala Gly Gln Leu Ala
            180                 185                 190

Ala Gly Ser His Ser Val Tyr Ala Arg Ala Tyr Asp Ser Leu Gly Ala
        195                 200                 205

Ser Ala Asp Ser Pro Pro Ala Gly Ile Thr Val Val Thr Gly Pro Ala
    210                 215                 220

Val Val Val Ser Pro Ala Gln Leu Gly Val Gln Gln Gly Arg Ser Gly
225                 230                 235                 240

Thr Phe Asp Val Ser Leu Ser Thr Ala Pro Ala Ala Asp Val Thr Val
                245                 250                 255

Thr Ala Ala Arg Ser Ala Gly Asn Thr Gly Leu Ser Val Thr Gly Gly
            260                 265                 270

Ser Thr Leu Thr Phe Thr Pro Ala Asn Trp Ser Thr Pro Gln Lys Val
        275                 280                 285

Thr Val Thr Ala Asp Gly Ser Gly Thr Gly Ala Ala Thr Phe Thr Val
    290                 295                 300

Thr Ala Pro Gly His Gly Lys Ala Glu Val Thr Val Thr Gln Leu Ala
305                 310                 315                 320

Ala Ala Lys Glu Tyr Asp Ala Arg Phe Leu Asp Leu Tyr Gly Lys Ile
                325                 330                 335

Thr Asp Pro Ala Asn Gly Tyr Phe Ser Pro Glu Gly Ile Pro Tyr His
            340                 345                 350

Ser Val Glu Thr Leu Ile Val Glu Ala Pro Asp His Gly His Glu Thr
        355                 360                 365

Thr Ser Glu Ala Tyr Ser Tyr Leu Ile Trp Leu Gln Ala Met Tyr Gly
    370                 375                 380

Lys Ile Thr Gly Asp Trp Thr Lys Phe Asn Gly Ala Trp Asp Thr Met
385                 390                 395                 400

Glu Thr Tyr Met Ile Pro Thr His Ala Asp Gln Pro Thr Asn Ser Phe
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                405                 410                 415

Tyr Asp Ala Ser Lys Pro Ala Thr Tyr Ala Pro Glu His Asp Thr Pro
            420                 425                 430

Asn Glu Tyr Pro Ala Val Leu Asp Gly Ser Ala Ser Ser Gly Ser Asp
        435                 440                 445

Pro Ile Ala Ala Glu Leu Lys Ser Ala Tyr Gly Thr Asp Asp Ile Tyr
    450                 455                 460

Gly Met His Trp Ile Gln Asp Val Asp Asn Val Tyr Gly Tyr Gly Asn
465                 470                 475                 480

Ala Pro Gly Thr Cys Ala Ala Gly Pro Thr Gln Ala Gly Pro Ser Tyr
                485                 490                 495

Ile Asn Thr Phe Gln Arg Gly Ser Gln Glu Ser Val Trp Glu Thr Val
            500                 505                 510

Thr His Pro Thr Cys Asp Asn Phe Thr Tyr Gly Gly Ala Asn Gly Tyr
        515                 520                 525

Leu Asp Leu Phe Thr Gly Asp Ser Ser Tyr Ala Lys Gln Trp Lys Phe
    530                 535                 540

Thr Asn Ala Pro Asp Ala Asp Ala Arg Ala Val Gln Ala Ala Tyr Trp
545                 550                 555                 560

Ala Asp Val Trp Ala Lys Glu Gln Gly Lys Ala Gly Glu Val Ala Asp
                565                 570                 575

Thr Val Gly Lys Ala Ala Lys Met Gly Asp Tyr Leu Arg Tyr Ser Met
            580                 585                 590

Phe Asp Lys Tyr Phe Lys Lys Ile Gly Asp Cys Val Gly Pro Thr Thr
        595                 600                 605

Cys Pro Ala Gly Ser Gly Lys Asp Ser Ala His Tyr Leu Met Ser Trp
    610                 615                 620

Tyr Tyr Ala Trp Gly Gly Ala Thr Asp Thr Ser Ala Gly Trp Ser Trp
625                 630                 635                 640

Arg Ile Gly Ser Ser His Ala His Gly Gly Tyr Gln Asn Pro Met Ala
                645                 650                 655

Ala Tyr Ala Leu Ser Ser Val Ala Asp Leu Lys Pro Lys Ser Ala Thr
            660                 665                 670

Gly Ala Gln Asp Trp Ala Lys Ser Leu Asp Arg Gln Leu Asp Phe Tyr
        675                 680                 685

Gln Trp Leu Gln Ser Asp Glu Gly Ala Ile Ala Gly Gly Ala Thr Asn
    690                 695                 700

Ser Trp Lys Gly Ser Tyr Ala Gln Pro Pro Ala Gly Thr Pro Thr Phe
705                 710                 715                 720

Tyr Gly Met Tyr Tyr Asp Glu Lys Pro Val Tyr His Asp Pro Pro Ser
                725                 730                 735

Asn Gln Trp Phe Gly Phe Gln Ala Trp Ser Met Glu Arg Val Ala Glu
            740                 745                 750

Tyr Tyr His Glu Ser Gly Asp Ala Gln Ala Lys Ala Val Leu Asp Lys
        755                 760                 765

Trp Val Asp Trp Ala Leu Ser Glu Thr Thr Val Asn Pro Asp Gly Thr
    770                 775                 780

Tyr Leu Met Pro Ser Thr Leu Gln Trp Ser Gly Ala Pro Asp Thr Trp
785                 790                 795                 800

Asn Ala Ser Asn Pro Gly Ala Asn Ala Gln Leu His Val Thr Val Ala
                805                 810                 815

Asp Tyr Thr Asp Asp Val Gly Val Ala Gly Ala Tyr Ala Arg Thr Leu
            820                 825                 830
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Thr Tyr Tyr Ala Ala Lys Ser Gly Asp Thr Glu Ala Glu Ala Thr Ala
        835                 840                 845

Glu Ala Leu Leu Asp Gly Met Trp Gln His His Gln Asp Asp Ala Gly
    850                 855                 860

Val Ala Val Pro Glu Thr Arg Ala Asp Tyr Asn Arg Phe Asp Asp Pro
865                 870                 875                 880

Val Tyr Val Pro Gly Gly Trp Thr Gly Ala Met Pro Asn Gly Asp Thr
                885                 890                 895

Val Asp Glu Asp Ser Thr Phe Leu Ser Ile Arg Ser Phe Tyr Lys Asp
            900                 905                 910

Asp Pro Asn Trp Pro Gln Val Gln Ala Tyr Leu Asp Gly Gly Ala Ala
        915                 920                 925

Pro Val Phe Thr Tyr His Arg Phe Trp Ala Gln Ala Asp Ile Ala Leu
    930                 935                 940

Ala Leu Gly Ala Tyr Ala Asp Leu Leu Glu
945                 950


<210> SEQ ID NO 9
<211> LENGTH: 586
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 9

Met Ser Arg Thr Ser Arg Thr Thr Leu Arg Arg Ser Arg Thr Ala Leu
1               5                   10                  15

Met Ala Ala Gly Ala Leu Val Ala Ala Ala Ala Gly Ser Ala Ala Ala
            20                  25                  30

Ala Ala Pro Phe Gly Ala Thr Ala Ala Ala Ala Ala Gly Cys Thr Val
        35                  40                  45

Asp Tyr Lys Ile Gln Asn Gln Trp Asn Gly Gly Leu Thr Ala Ser Val
    50                  55                  60

Ser Val Thr Asn Asn Gly Asp Ala Ile Ser Gly Trp Gln Leu Gln Trp
65                  70                  75                  80

Ser Phe Ala Gly Gly Glu Gln Val Ser Gln Gly Trp Asn Ala Thr Val
                85                  90                  95

Ser Gln Ser Gly Ser Ala Val Thr Ala Lys Asp Ala Gly Tyr Asn Ala
            100                 105                 110

Ala Leu Ala Thr Gly Ala Ser Ala Ser Phe Gly Phe Asn Ala Thr Gly
        115                 120                 125

Asn Gly Asn Ser Val Val Pro Ala Thr Phe Lys Leu Asn Gly Val Thr
    130                 135                 140

Cys Asn Gly Gly Thr Thr Gly Pro Thr Asp Pro Thr Asp Pro Thr Asp
145                 150                 155                 160

Pro Thr Asp Pro Thr Asp Pro Pro Ala Gly Asn Arg Val Asp Asn Pro
                165                 170                 175

Tyr Gln Gly Ala Lys Val Tyr Val Asn Pro Glu Trp Ser Ala Asn Ala
            180                 185                 190

Ala Ala Glu Pro Gly Gly Asp Arg Ile Ala Asp Gln Pro Thr Gly Val
        195                 200                 205

Trp Leu Asp Arg Ile Ala Ala Ile Glu Gly Ala Asn Gly Ser Met Gly
    210                 215                 220

Leu Arg Asp His Leu Asp Glu Ala Leu Thr Gln Lys Gly Ser Gly Glu
225                 230                 235                 240

Leu Val Val Gln Val Val Ile Tyr Asn Leu Pro Gly Arg Asp Cys Ala
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               245                 250                 255

Ala Leu Ala Ser Asn Gly Glu Leu Gly Pro Thr Glu Ile Gly Arg Tyr
            260                 265                 270

Lys Thr Glu Tyr Ile Asp Pro Ile Ala Glu Ile Leu Gly Asp Pro Lys
        275                 280                 285

Tyr Ala Gly Leu Arg Ile Val Thr Thr Val Glu Ile Asp Ser Leu Pro
    290                 295                 300

Asn Leu Val Thr Asn Ala Gly Gly Arg Pro Thr Ala Thr Pro Ala Cys
305                 310                 315                 320

Asp Val Met Lys Ala Asn Gly Asn Tyr Val Lys Gly Val Gly Tyr Ala
                325                 330                 335

Leu Asn Lys Leu Gly Asp Ala Pro Asn Val Tyr Asn Tyr Ile Asp Ala
            340                 345                 350

Gly His His Gly Trp Ile Gly Trp Asp Asp Asn Phe Gly Ala Ser Ala
        355                 360                 365

Glu Ile Phe His Glu Ala Ala Thr Ala Glu Gly Ala Thr Val Asn Asp
    370                 375                 380

Val His Gly Phe Ile Thr Asn Thr Ala Asn Tyr Ser Ala Leu Lys Glu
385                 390                 395                 400

Glu Asn Phe Ser Ile Asp Asp Ala Val Asn Gly Thr Ser Val Arg Gln
                405                 410                 415

Ser Lys Trp Val Asp Trp Asn Arg Tyr Thr Asp Glu Leu Ser Phe Ala
            420                 425                 430

Gln Ala Phe Arg Asn Glu Leu Val Ser Val Gly Phe Asn Ser Gly Ile
        435                 440                 445

Gly Met Leu Ile Asp Thr Ser Arg Asn Gly Trp Gly Gly Ala Asn Arg
    450                 455                 460

Pro Ser Gly Pro Gly Ala Asn Thr Ser Val Asp Thr Tyr Val Asp Gly
465                 470                 475                 480

Gly Arg Tyr Asp Arg Arg Ile His Leu Gly Asn Trp Cys Asn Gln Ala
                485                 490                 495

Gly Ala Gly Leu Gly Glu Arg Pro Gln Ala Ala Pro Glu Pro Gly Ile
            500                 505                 510

Asp Ala Tyr Val Trp Met Lys Pro Pro Gly Glu Ser Asp Gly Ser Ser
        515                 520                 525

Ser Glu Ile Pro Asn Asp Glu Gly Lys Gly Phe Asp Arg Met Cys Asp
    530                 535                 540

Pro Thr Tyr Thr Gly Asn Ala Arg Asn Asn Asn Asn Met Ser Gly Ala
545                 550                 555                 560

Leu Gly Gly Ala Pro Val Ser Gly Lys Trp Phe Ser Ala Gln Phe Gln
                565                 570                 575

Glu Leu Met Lys Asn Ala Tyr Pro Ala Leu
            580                 585


<210> SEQ ID NO 10
<211> LENGTH: 362
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 10

Met Ala Arg Arg Ser Arg Leu Ile Ser Leu Ala Ala Val Leu Ala Thr
1               5                   10                  15

Leu Leu Gly Ala Leu Gly Leu Thr Ala Leu Trp Pro Gly Lys Ala Glu
            20                  25                  30
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Ala His Gly Val Ala Met Thr Pro Gly Ser Arg Thr Tyr Leu Cys Gln
        35                  40                  45

Leu Asp Ala Leu Ser Gly Thr Gly Ala Leu Asn Pro Thr Asn Pro Ala
    50                  55                  60

Cys Arg Asp Ala Leu Ser Gln Ser Gly Ala Asn Ala Leu Tyr Asn Trp
65                  70                  75                  80

Phe Ala Val Leu Asp Ser Asn Ala Gly Gly Arg Gly Ala Gly Tyr Val
                85                  90                  95

Pro Asp Gly Ser Leu Cys Ser Ala Gly Asp Arg Ser Pro Tyr Asp Phe
            100                 105                 110

Ser Ala Tyr Asn Ala Ala Arg Ala Asp Trp Pro Arg Thr His Leu Thr
        115                 120                 125

Ser Gly Ala Thr Leu Lys Val Gln Tyr Ser Asn Trp Ala Ala His Pro
    130                 135                 140

Gly Asp Phe Arg Val Tyr Leu Thr Lys Pro Gly Trp Ala Pro Thr Ser
145                 150                 155                 160

Glu Leu Ala Trp Asp Asp Leu Gln Leu Val Gln Thr Val Ser Asn Pro
                165                 170                 175

Pro Gln Gln Gly Gly Ala Gly Thr Asn Gly Gly His Tyr Tyr Trp Asp
            180                 185                 190

Leu Ala Leu Pro Ser Gly Arg Ser Gly Asp Ala Leu Met Phe Ile Gln
        195                 200                 205

Trp Val Arg Ser Asp Ser Gln Glu Asn Phe Phe Ser Cys Ser Asp Ile
    210                 215                 220

Val Phe Asp Gly Gly Asn Gly Glu Val Thr Gly Ile Gly Gly Thr Gly
225                 230                 235                 240

Thr Pro Thr Pro Thr Pro Thr Pro Thr Pro Thr Pro Thr Pro Thr Asp
                245                 250                 255

Pro Glu His Ser Gly Ser Cys Met Ala Val Tyr Asn Val Val Ser Ser
            260                 265                 270

Trp Ala Gly Gly Phe Gln Ala Ser Val Glu Val Met Asn His Gly Thr
        275                 280                 285

Glu Pro Arg Asn Gly Trp Ala Val Gln Trp Lys Pro Gly Ser Gly Thr
    290                 295                 300

Gln Ile Asn Ser Val Trp Asn Gly Ser Leu Ser Thr Gly Ser Asp Gly
305                 310                 315                 320

Thr Val Thr Val Arg Asp Val Asp His Asn Arg Val Ile Ala Pro Asp
                325                 330                 335

Gly Ser Val Thr Phe Gly Phe Thr Ala Thr Ser Thr Gly Asn Asp Tyr
            340                 345                 350

Pro Ala Gly Thr Ile Gly Cys Val Thr Ser
        355                 360


<210> SEQ ID NO 11
<211> LENGTH: 909
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 11

Met Trp Cys His Pro Tyr Leu Arg Leu Arg Thr Ser Gly Arg Lys Val
1               5                   10                  15

Ser Ser Val Asn Ala Leu Pro Pro Pro Ala Arg Pro Ala Pro Val Arg
            20                  25                  30

Pro Arg Ser Arg Tyr Gly Arg Arg Val Leu Gly Met Ser Ala Ala Ala
        35                  40                  45
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Leu Leu Cys Ala Gly Ala Leu Ala Val Pro Gly Thr Ala Met Ala Asp
    50                  55                  60

Asp Ala Glu Pro Gly Pro Gly Pro Glu Gln Ile Thr Asn Gly Asp Phe
65                  70                  75                  80

Ala Thr Gly Thr Ser Ala Pro Trp Trp Trp Thr Pro Asn Ala Ser Ala
                85                  90                  95

Ala Val Ser Glu Gly Arg Leu Cys Val Glu Val Pro Ala Gly Thr Ala
            100                 105                 110

Asn Ala Trp Asp Val Ile Val Gly Gln Asn Asp Val Pro Ile Val Ala
        115                 120                 125

Gly Glu Ser Tyr Glu Leu Ser Tyr Thr Ala Arg Ser Thr Val Pro Leu
    130                 135                 140

Thr Val Gln Thr Arg Val Gln Glu Ala Val Glu Pro Tyr Thr Thr Val
145                 150                 155                 160

Leu Ala Thr Ala Asp Pro Val Gly Ala Glu Asp Thr Arg Val Ala Arg
                165                 170                 175

Thr Phe Thr Ala Ser Val Asp Gln Pro Ala Ala Ser Val Gln Leu Gln
            180                 185                 190

Ile Gly Gly Gly Glu Arg Ala Thr Thr Phe Cys Leu Asp Asp Val Ser
        195                 200                 205

Leu Arg Gly Gly Ala Glu Pro Pro Val Tyr Val Pro Asp Thr Gly Ser
    210                 215                 220

Pro Val Arg Val Asn Gln Val Gly Tyr Leu Pro Arg Gly Pro Lys Ser
225                 230                 235                 240

Gly Thr Val Val Thr Asp Ala Glu Ala Pro Leu Thr Trp Thr Val Lys
                245                 250                 255

Ala Glu Asp Gly Ser Thr Ala Ala Thr Gly Thr Thr Val Pro Arg Gly
            260                 265                 270

Glu Asp Pro Ser Ser Arg Arg Arg Val His Thr Phe Asp Phe Gly Asp
        275                 280                 285

Leu Thr Thr Ala Gly Asp Gly Tyr Thr Val Glu Val Asp Gly Glu Val
    290                 295                 300

Ser Glu Pro Phe Ser Ile Arg Gly Asp Leu Tyr Asp Ser Leu Arg Ser
305                 310                 315                 320

Asp Ala Leu Ala Tyr Phe Tyr His Asn Arg Ser Gly Ile Glu Ile Asp
                325                 330                 335

Ala Asp Leu Val Gly Glu Gln Tyr Ala Arg Pro Ala Gly His Ile Gly
            340                 345                 350

Val Ala Pro Asn Lys Gly Asp Thr Asp Val Pro Cys Arg Pro Gly Val
        355                 360                 365

Cys Asp Tyr Arg Leu Asp Val Ser Gly Gly Trp Tyr Asp Ala Gly Asp
    370                 375                 380

His Gly Lys Tyr Val Val Asn Gly Gly Ile Ser Val Ala Gln Leu Met
385                 390                 395                 400

Ala Thr Tyr Glu Arg Thr Leu Thr Ala Pro Asp Ala Glu Ser Ala Glu
                405                 410                 415

Leu Gly Asp Gly Ala Leu Arg Val Pro Glu Arg Asp Asn Gly Val Pro
            420                 425                 430

Asp Ile Leu Asp Glu Ala Arg Trp Glu Met Asp Phe Leu Ile Lys Met
        435                 440                 445

Gln Val Pro Ala Gly Glu Gln Leu Ala Gly Met Val His His Lys Met
    450                 455                 460
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His Asp Ala Glu Trp Thr Gly Leu Pro Met Lys Pro His Leu Asp Pro
465                 470                 475                 480

Gln Gln Arg Glu Leu His Pro Pro Ser Thr Ala Ala Thr Leu Asn Leu
                485                 490                 495

Ala Ala Thr Ala Ala Gln Cys Ala Arg Leu Tyr Ala Pro Phe Asp Ala
            500                 505                 510

Asp Phe Ala Asp Arg Cys Leu Arg Ala Ala Glu Thr Ala Trp Asp Ala
        515                 520                 525

Ala Lys Arg His Pro Asp Val Leu Ala Asp Pro Asn Asp Gly Ile Gly
    530                 535                 540

Gly Gly Ala Tyr Asn Asp Asp Asp Val Ser Asp Glu Phe Tyr Trp Ala
545                 550                 555                 560

Ala Ala Glu Leu Phe Thr Thr Thr Gly Lys Asp Ile Tyr Arg Gln Ala
                565                 570                 575

Val Leu Ser Ser Ala Trp His Gly Asp Ala Gly Ala Val Phe Pro Ala
            580                 585                 590

Gly Gly Gly Ile Ser Trp Gly Ser Thr Ala Gly Leu Gly Val Leu Thr
        595                 600                 605

Leu Ala Thr Val Pro Asn Ala Leu Thr Ser Asp Gln Leu Ala Gln Val
    610                 615                 620

Arg Thr Val Val Thr Glu Gly Ala Asp Arg Tyr Ala Ala Gln Ser Arg
625                 630                 635                 640

Glu Gln Ala Tyr Gly Leu Pro Tyr Ala Pro Arg Gly Glu Asp Tyr Val
                645                 650                 655

Trp Gly Ser Asn Ser Gln Val Leu Asn Asn Met Val Val Leu Ala Thr
            660                 665                 670

Ala His Asp Leu Thr Gly Asp Ala Ala Tyr Gln Asp Ala Val Leu Arg
        675                 680                 685

Gly Ala Asp Tyr Leu Leu Gly Arg Asn Pro Leu Asn Gln Ser Tyr Val
    690                 695                 700

Thr Gly Tyr Gly Glu Arg Asp Ser His Asn Gln His His Arg Phe Trp
705                 710                 715                 720

Ala His Gln Asn Asp Pro Ser Leu Pro Asn Pro Ala Pro Gly Ser Ile
                725                 730                 735

Ala Gly Gly Pro Asn Leu Thr Ala Ile Ala Ser Gly Asp Pro Val Ala
            740                 745                 750

Ala Glu Lys Leu Ser Gly Cys Ala Pro Ala Met Cys Tyr Val Asp Asp
        755                 760                 765

Ile Gly Ser Trp Ala Thr Asn Glu Ile Thr Ile Asn Trp Asn Ala Pro
    770                 775                 780

Leu Ala Phe Ile Ala Ser Tyr Leu Asp Asp Ala Gly Glu Gly Gly Gln
785                 790                 795                 800

Thr Ala Ala Ala Arg Thr Cys Gln Val Thr Tyr Ser Ser His Pro Trp
                805                 810                 815

Asn Ser Gly Ser Thr Val Thr Val Arg Val Glu Asn Thr Gly Ser Asp
            820                 825                 830

Pro Val Ser Pro Trp Ala Leu Thr Trp Leu Leu Pro Gly Glu Gln Arg
        835                 840                 845

Leu Ser His Thr Trp Ser Ala Glu Phe Asp Gln His Gly Arg Thr Val
    850                 855                 860

Ser Ala Arg Pro Leu Ser Trp Asn Arg Thr Leu Ala Pro Gly Ala Ala
865                 870                 875                 880

Val Asp Phe Gly Phe Asn Thr Ser Ala Ala Gly Ser Ser Pro Glu Pro
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                885                 890                 895

Gly Ala Phe Lys Leu Asn Gly Arg Ala Cys Ser Ala Gly
            900                 905


<210> SEQ ID NO 12
<211> LENGTH: 456
<212> TYPE: PRT
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 12

Met Lys Arg Phe Leu Ala Leu Leu Ala Thr Cys Ala Thr Val Leu Gly
1               5                   10                  15

Leu Thr Ala Leu Thr Gly Pro Gln Ala Val Ala Ala Ala Gly Cys Thr
            20                  25                  30

Ala Asp Tyr Thr Ile Thr Ser Gln Trp Gln Gly Gly Phe Gln Ala Ala
        35                  40                  45

Val Lys Val Thr Asn Leu Gly Thr Pro Val Thr Gly Trp Lys Leu Thr
    50                  55                  60

Phe Thr Leu Pro Asp Ala Gly Gln Lys Val Val Gln Gly Trp Asn Ala
65                  70                  75                  80

Ala Trp Ser Gln Ser Gly Ser Ala Val Thr Ala Ala Gly Ala Asp Trp
                85                  90                  95

Asn Gly Thr Leu Ala Thr Gly Ala Ser Ala Glu Ala Gly Phe Val Gly
            100                 105                 110

Ser Phe Thr Gly Ala Asn Pro Pro Pro Thr Ala Phe Ala Leu Asn Gly
        115                 120                 125

Val Ala Cys Thr Gly Ser Thr Gly Glu Pro Pro Ala Gly Ser Asp Gly
    130                 135                 140

Gly Thr Pro Val Asp Val Asn Gly Gln Leu His Val Cys Gly Val Asn
145                 150                 155                 160

Leu Cys Asn Gln Tyr Asp Arg Pro Val Gln Leu Arg Gly Met Ser Thr
                165                 170                 175

His Gly Ile Gln Trp Phe Asp Ala Cys Tyr Asp Ala Ala Ser Leu Asp
            180                 185                 190

Ala Leu Ala Asn Asp Trp Lys Ser Asp Leu Leu Arg Ile Ala Met Tyr
        195                 200                 205

Val Gln Glu Asp Gly Tyr Glu Thr Asp Pro Ala Gly Phe Thr Arg Arg
    210                 215                 220

Val Asn Asp Leu Val Asp Met Ala Glu Ala Arg Gly Met Tyr Ala Leu
225                 230                 235                 240

Ile Asp Phe His Thr Leu Thr Pro Gly Asp Pro Asn Val Asn Leu Asp
                245                 250                 255

Arg Ala Lys Thr Phe Phe Ala Ser Val Ala Ala Arg Asn Ala Gly Lys
            260                 265                 270

Lys Asn Val Ile Tyr Glu Ile Ala Asn Glu Pro Asn Gly Val Thr Trp
        275                 280                 285

Thr Ala Val Lys Ser Tyr Ala Glu Gln Val Ile Pro Val Ile Arg Ala
    290                 295                 300

Ala Asp Pro Asp Ala Val Val Ile Val Gly Thr Arg Gly Trp Ser Ser
305                 310                 315                 320

Leu Gly Val Ser Asp Gly Ser Asp Glu Ser Glu Val Val Asn Ser Pro
                325                 330                 335

Val Asn Ala Thr Asn Ile Met Tyr Ala Phe His Phe Tyr Ala Ala Ser
            340                 345                 350
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His Lys Asp Ala Tyr Arg Ser Thr Leu Ser Arg Ala Ala Ala Arg Leu
        355                 360                 365

Pro Leu Phe Val Thr Glu Phe Gly Thr Val Ser Ala Thr Gly Gly Gly
    370                 375                 380

Ala Met Asp Arg Ala Ser Thr Thr Ala Trp Leu Asp Leu Leu Asp Gln
385                 390                 395                 400

Leu Lys Ile Ser Tyr Ala Asn Trp Thr Tyr Ser Asp Ala Pro Glu Ser
                405                 410                 415

Ser Ala Ala Phe Arg Pro Gly Thr Cys Gly Gly Gly Asp Tyr Ser Gly
            420                 425                 430

Ser Gly Val Leu Thr Glu Ser Gly Ala Leu Leu Lys Asn Arg Ile Ser
        435                 440                 445

Thr Pro Asp Ser Phe Pro Thr Gly
    450                 455


<210> SEQ ID NO 13
<211> LENGTH: 583
<212> TYPE: PRT
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 13

Met Ser Arg Thr Ser Arg Thr Thr Leu Arg Arg Ser Arg Thr Ala Leu
1               5                   10                  15

Ile Ala Ala Gly Ala Leu Val Ala Ala Ala Ala Gly Ser Ala Ala Ala
            20                  25                  30

Ala Ala Pro Phe Ala Ala Ser Ala Ala Ala Ala Thr Gly Cys Thr Val
        35                  40                  45

Asp Tyr Lys Ile Glu Asn Gln Trp Asn Gly Gly Leu Thr Ala Ala Val
    50                  55                  60

Asn Val Thr Asn Asn Gly Ala Pro Val Thr Ser Trp Gln Leu Gln Trp
65                  70                  75                  80

Thr Phe Asn Gly Gly Glu Gln Val Ser Gln Gly Trp Asn Ala Thr Ile
                85                  90                  95

Ser Gln Ser Gly Ser Ala Val Thr Ala Lys Asp Ala Gly Tyr Asn Gly
            100                 105                 110

Thr Leu Ala Thr Gly Ala Ser Ala Ser Phe Gly Phe Asn Ala Thr Gly
        115                 120                 125

Asn Gly Asn Ser Thr Val Pro Ala Thr Phe Lys Leu Asn Gly Val Thr
    130                 135                 140

Cys Asn Gly Asp Thr Thr Gly Pro Thr Asp Pro Thr Asp Pro Thr Asp
145                 150                 155                 160

Pro Thr Asp Pro Pro Ala Gly Asn Arg Val Asp Asn Pro Tyr Gln Gly
                165                 170                 175

Ala Lys Val Tyr Val Asn Pro Glu Trp Ser Ala Asn Ala Ala Ala Glu
            180                 185                 190

Pro Gly Gly Ser Arg Val Ala Asn Gln Pro Thr Gly Val Trp Leu Asp
        195                 200                 205

Arg Ile Ala Ala Ile Glu Gly Ala Asn Gly Ser Met Gly Leu Arg Glu
    210                 215                 220

His Leu Asp Glu Ala Leu Thr Gln Lys Gly Ser Gly Glu Leu Val Val
225                 230                 235                 240

Gln Leu Val Ile Tyr Asp Leu Pro Gly Arg Asp Cys Ala Ala Leu Ala
                245                 250                 255

Ser Asn Gly Glu Leu Gly Pro Thr Glu Ile Gly Arg Tyr Lys Thr Glu
            260                 265                 270
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Tyr Ile Asp Pro Ile Ala Ala Ile Val Ala Asp Pro Lys Tyr Ala Gly
        275                 280                 285

Leu Arg Ile Val Thr Thr Val Glu Ile Asp Ser Leu Pro Asn Leu Val
    290                 295                 300

Thr Asn Ala Gly Gly Arg Glu Thr Ala Thr Pro Ala Cys Asp Val Met
305                 310                 315                 320

Lys Ala Asn Gly Asn Tyr Val Lys Gly Val Gly Tyr Ala Leu Asn Lys
                325                 330                 335

Leu Gly Asp Ala Pro Asn Val Tyr Asn Tyr Ile Asp Ala Gly His His
            340                 345                 350

Gly Trp Ile Gly Trp Asp Asp Asn Phe Gly Ala Ser Ala Gln Ile Phe
        355                 360                 365

His Glu Ala Ala Thr Ala Glu Gly Ala Thr Val Asn Asp Val His Gly
    370                 375                 380

Phe Ile Thr Asn Thr Ala Asn Tyr Ser Ala Leu Lys Glu Gln Asn Phe
385                 390                 395                 400

Ser Ile Asn Asp Ser Val Asn Gly Thr Ser Val Arg Glu Ser Lys Trp
                405                 410                 415

Val Asp Trp Asn Arg Tyr Thr Asp Glu Leu Ser Phe Ala Gln Ala Phe
            420                 425                 430

Arg Asn Glu Leu Val Ser Val Gly Phe Asn Ser Gly Ile Gly Met Leu
        435                 440                 445

Ile Asp Thr Ser Arg Asn Gly Trp Gly Gly Ser Ala Arg Pro Ser Gly
    450                 455                 460

Pro Gly Ala Thr Thr Ser Val Asp Thr Tyr Val Asp Gly Gly Arg Tyr
465                 470                 475                 480

Asp Arg Arg Ile His Leu Gly Asn Trp Cys Asn Gln Ala Gly Ala Gly
                485                 490                 495

Leu Gly Glu Arg Pro Thr Ala Ala Pro Glu Pro Gly Ile Asp Ala Tyr
            500                 505                 510

Val Trp Met Lys Pro Pro Gly Glu Ser Asp Gly Ser Ser Ser Glu Ile
        515                 520                 525

Pro Asn Asp Glu Gly Lys Gly Phe Asp Arg Met Cys Asp Pro Thr Tyr
    530                 535                 540

Thr Gly Asn Pro Arg Asn Asn Asn Asn Pro Ser Gly Ala Leu Gly Gly
545                 550                 555                 560

Ala Pro Val Ser Gly Lys Trp Phe Ser Ala Gln Phe Gln Glu Leu Met
                565                 570                 575

Lys Asn Ala Tyr Pro Ala Leu
            580


<210> SEQ ID NO 14
<211> LENGTH: 888
<212> TYPE: PRT
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 14

Met Asn Ala Leu Pro Pro Pro Ala Arg Pro Ala Pro Val Arg Ser Arg
1               5                   10                  15

Ser Arg Tyr Gly Arg Arg Ala Leu Gly Ile Ser Ala Ala Ala Leu Leu
            20                  25                  30

Cys Ala Gly Ala Leu Ala Val Pro Gly Thr Ala Leu Ala Asp Asp Ala
        35                  40                  45

Ala Pro Gly Pro Glu Gln Ile Thr Asn Gly Asp Phe Ser Ala Gly Thr
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    50                  55                  60

Ala Pro Trp Trp Trp Thr Pro Asn Ala Ser Ala Ala Val Ser Glu Gly
65                  70                  75                  80

Arg Leu Cys Val Glu Val Pro Ala Gly Thr Ala Glu Ala Trp Asp Val
                85                  90                  95

Ile Val Gly Gln Asn Asp Ile Pro Ile Val Ala Gly Glu Ser Tyr Glu
            100                 105                 110

Leu Ser Tyr Thr Ala Arg Ser Thr Val Pro Leu Thr Val Gln Thr Arg
        115                 120                 125

Val Gln Glu Ala Val Glu Pro Tyr Gly Thr Val Leu Ala Thr Ala Asp
    130                 135                 140

Pro Val Gly Thr Glu Asp Thr Gln Val Thr Arg Thr Phe Thr Ala Ser
145                 150                 155                 160

Val Asp Gln Pro Ala Ala Ser Val Gln Leu Gln Ile Gly Gly Gly Glu
                165                 170                 175

Arg Ala Thr Thr Phe Cys Leu Asp Asp Val Ser Leu Arg Gly Gly Ala
            180                 185                 190

Glu Pro Pro Val Tyr Val Pro Asp Thr Gly Ser Pro Val Arg Val Asn
        195                 200                 205

Gln Val Gly Tyr Leu Pro Arg Gly Val Lys Ser Gly Thr Val Val Thr
    210                 215                 220

Asp Ala Glu Ala Pro Leu Thr Trp Thr Val Lys Ala Gly Asp Gly Ser
225                 230                 235                 240

Thr Ala Ala Thr Gly Thr Thr Val Pro Arg Gly Glu Asp Pro Ser Ser
                245                 250                 255

Arg Gln Arg Val His Thr Phe Asp Phe Gly Gly Leu Thr Thr Pro Gly
            260                 265                 270

Asp Gly Tyr Thr Val Glu Val Asp Gly Glu Val Ser Glu Pro Phe Ser
        275                 280                 285

Ile Arg Gly Asp Leu Tyr Asp Gly Leu Arg Ser Asp Ala Leu Ala Tyr
    290                 295                 300

Phe Tyr His Asn Arg Ser Gly Ile Glu Ile Asp Ala Asp Leu Val Gly
305                 310                 315                 320

Glu Glu Tyr Ala Arg Pro Ala Gly His Ile Gly Val Ala Pro Asn Lys
                325                 330                 335

Gly Asp Thr Asp Val Pro Cys Lys Pro Gly Val Cys Asp Tyr Arg Leu
            340                 345                 350

Asp Val Ser Gly Gly Trp Tyr Asp Ala Gly Asp His Gly Lys Tyr Val
        355                 360                 365

Val Asn Gly Gly Ile Ser Val Ala Gln Leu Met Ser Thr Tyr Glu Arg
    370                 375                 380

Thr Leu Thr Ala Asp Asn Ala Glu Ser Ala Gln Leu Asp Asp Gly Ala
385                 390                 395                 400

Leu Arg Val Pro Glu Arg Gly Asn Gly Val Pro Asp Ile Leu Asp Glu
                405                 410                 415

Ala Arg Trp Glu Met Asp Phe Leu Ile Lys Met Gln Val Pro Ala Gly
            420                 425                 430

Glu Pro Leu Ala Gly Met Val His His Lys Met His Asp Ala Glu Trp
        435                 440                 445

Thr Gly Leu Pro Met Lys Pro His Leu Asp Pro Gln Gln Arg Glu Leu
    450                 455                 460

His Ala Pro Ser Thr Ala Ala Thr Leu Asn Leu Ala Ala Thr Ala Ala
465                 470                 475                 480
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```
Gln Cys Ala Arg Leu Tyr Ala Pro Tyr Asp Glu Asp Phe Ala Asp Arg
                485                 490                 495

Cys Leu Arg Ala Ala Glu Thr Ala Trp Asp Ala Ala Lys Arg His Pro
            500                 505                 510

Asp Val Phe Ala Asp Pro Asn Asp Gly Val Gly Gly Gly Thr Tyr Asp
        515                 520                 525

Asp Asn Asp Val Ser Asp Glu Phe Tyr Trp Ala Ala Ala Glu Leu Phe
    530                 535                 540

Thr Thr Thr Gly Lys Asp Thr Tyr Arg Gln Glu Val Leu Ser Ser Asp
545                 550                 555                 560

Leu His Gly Asp Ala Asp Ala Val Phe Pro Ala Gly Gly Gly Leu Ser
                565                 570                 575

Trp Gly Ala Thr Ala Gly Leu Gly Ala Leu Thr Leu Ala Thr Val Pro
            580                 585                 590

Asn Asn Leu Thr Thr Asp Gln Leu Asp Gly Val Arg Ala Thr Val Thr
        595                 600                 605

Thr Ala Ala Asp Arg Tyr Ala Ala Gln Ser Arg Ala Gln Ala Tyr Gly
    610                 615                 620

Leu Pro Tyr Ala Pro Arg Gly Thr Asp Tyr Val Trp Gly Ser Asn Ser
625                 630                 635                 640

Gln Val Leu Asn Asn Met Val Val Leu Ala Val Ala His Asp Leu Thr
                645                 650                 655

Gly Glu Ala Ala Tyr Gln Asp Ala Val Leu Arg Gly Ala Asp Tyr Leu
            660                 665                 670

Phe Gly Arg Asn Pro Leu Asn Gln Ser Tyr Val Thr Gly Tyr Gly Glu
        675                 680                 685

Arg Asp Ser His Asn Gln His His Arg Phe Trp Ala His Gln Tyr Asp
    690                 695                 700

Ser Ser Leu Pro Asn Pro Ala Pro Gly Ser Val Ala Gly Gly Pro Asn
705                 710                 715                 720

Leu Thr Ala Ala Gly Ser Gly Asp Pro Val Ala Ala Glu Lys Leu Ser
                725                 730                 735

Gly Cys Ala Pro Ala Met Cys Tyr Ile Asp Asp Ile Gly Ser Trp Ser
            740                 745                 750

Thr Asn Glu Ile Thr Val Asn Trp Asn Ala Pro Leu Ala Phe Ile Ala
        755                 760                 765

Ser Tyr Leu Asp Asp Ala Gly Asp Gly Gly Gln Thr Thr Ala Ser Arg
    770                 775                 780

Thr Cys Glu Val Thr Tyr Ser Ser His Pro Trp Ser Gly Gly Ser Thr
785                 790                 795                 800

Val Ser Val Arg Val Glu Asn Thr Gly Ser Ala Pro Val Glu Pro Trp
                805                 810                 815

Ser Leu Thr Trp Leu Leu Pro Gly Glu Gln Lys Leu Ser His Thr Trp
            820                 825                 830

Ser Ala Glu Phe Glu Gln His Gly Arg Thr Val Ser Ala Arg Pro Leu
        835                 840                 845

Ala Trp Asn Arg Thr Leu Ala Pro Gly Ala Ala Val Asp Phe Gly Phe
    850                 855                 860

Asn Thr Ser Ala Thr Gly Ala Ala Ala Asp Pro Gly Thr Phe Lys Leu
865                 870                 875                 880

Asn Gly Arg Ala Cys Ala Ser Gly
                885
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<210> SEQ ID NO 15
<211> LENGTH: 379
<212> TYPE: PRT
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 15

Met Lys Ser Leu Ile Ala Ser Leu Arg Ser Ala Gly Thr Ala Val Thr
1 5 10 15

Ala Ser Leu Val Ala Leu Ala Thr Cys Ala Ala Leu Gly Ala Leu Ala
20 25 30

Ala Pro Ala Gln Ala Ala Asp Ser Ile Cys Gly Gln Tyr Gly Thr Thr
35 40 45

Val Ile Gln Asp Arg Tyr Val Val Gln Asn Asn Arg Trp Gly Thr Thr
50 55 60

Asp Ala Gln Cys Val Asp Val Thr Asp Asp Gly Phe Thr Val Thr Arg
65 70 75 80

Ala Asp Gly Ser Val Pro Thr Asn Gly Ala Pro Lys Ser Tyr Pro Ser
85 90 95

Val Tyr Asn Gly Cys His Tyr Thr Asn Cys Ser Pro Gly Thr Glu Leu
100 105 110

Pro Lys Arg Leu Asp Ser Ile Ser Ser Ala Pro Thr Ala Ile Thr Tyr
115 120 125

Thr Tyr Val Asp Gly Ala Val Tyr Asp Ala Ala Tyr Asp Ile Trp Leu
130 135 140

Asp Pro Gln Pro Lys Lys Asp Gly Val Asn Arg Thr Glu Ile Met Ile
145 150 155 160

Trp Phe Asn Arg Val Gly Pro Ile Gln Pro Val Gly Ser Gln Thr Gly
165 170 175

Thr Ala Thr Val Ala Gly Arg Gly Trp Glu Val Trp Thr Gly Asn Asn
180 185 190

Gly Gly Asn Asp Val Ile Ser Phe Val Ser Pro Ser Ala Ile Ser Ser
195 200 205

Trp Ser Phe Asp Val Met Asp Phe Val Asp Ala Thr Val Ala Arg Gly
210 215 220

Met Ala Gln Asn Ser Trp Tyr Leu Thr Ser Val Gln Ala Gly Phe Glu
225 230 235 240

Pro Trp Gln Asn Gly Ala Gly Leu Ala Val Ser Ser Phe Ser Ser Ser
245 250 255

Val Leu Thr Gly Gly Gly Ser Glu Gly Pro Gly Glu Pro Gly Thr Pro
260 265 270

Ala Asp Gly Pro Cys Ala Val Ser Tyr Thr Ala Asn Ala Trp Thr Asp
275 280 285

Gly Phe Thr Ala Asp Val Lys Val Thr Asn Thr Gly Thr Val Pro Val
290 295 300

Ser Gly Trp Arg Leu Gly Phe Thr Leu Pro Gln Gly Gln Thr Val Thr
305 310 315 320

Gln Ala Trp Asn Ala Thr Val Thr Pro Ser Ser Gly Ala Val Thr Ala
325 330 335

Thr Gly Ala Ala Phe Asn Ala Glu Ile Ala Ala Gly Ala Ser Gln Ser
340 345 350

Phe Gly Phe Gln Gly Thr His Ser Gly Thr Phe Thr Lys Pro Asp Arg
355 360 365

Phe Thr Leu Asn Gly Ala Val Cys Thr Val Gly
370 375

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<210> SEQ ID NO 16
<211> LENGTH: 954
<212> TYPE: PRT
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 16

Met Ala Ala Leu Ala Leu Pro Leu Gly Met Thr Ala Ala Ala Gly Thr
1 5 10 15

Pro Ala Gln Ala Ala Ala Val Ala Cys Ser Val Asp Tyr Lys Ala Asn
20 25 30

Asp Trp Gly Ser Gly Phe Thr Thr Glu Leu Thr Leu Thr Asn Arg Gly
35 40 45

Ser Gly Ala Ile Asp Gly Trp Thr Leu Thr Tyr Asp Tyr Ala Gly Asn
50 55 60

Gln Gln Leu Thr Ser Gly Trp Ser Gly Val Trp Ser Gln Ser Gly Lys
65 70 75 80

Thr Val Thr Val Lys Asn Ala Asp Trp Asn Gly Thr Val Ala Ala Gly
85 90 95

Gln Ala Val Thr Ala Gly Ala Gln Phe Thr Tyr Ser Gly Thr Asn Thr
100 105 110

Asp Pro Thr Ala Phe Ala Val Asn Gly Thr Val Cys Ala Gly Ala His
115 120 125

Gln Pro Pro Ile Ala Val Leu Thr Ser Pro Ala Ala Gly Ala Val Phe
130 135 140

Thr Ala Gly Asp Pro Val Pro Leu Ala Ala Thr Ala Ala Ala Ala Asp
145 150 155 160

Gly Ala Thr Ile Ser Lys Val Glu Phe Tyr Asp Asn Thr Thr Leu Leu
165 170 175

Gly Thr Asp Thr Thr Ser Pro Tyr Ser Tyr Thr Ala Gln Gly Leu Ser
180 185 190

Ala Gly Ser His Ser Val Tyr Ala Arg Ala Tyr Asp Ser Leu Gly Ala
195 200 205

Ser Ala Glu Ser Pro Pro Ala Gly Ile Thr Val Ala Ala Gly Pro Ala
210 215 220

Val Val Ala Thr Pro Ala Gln Leu Gly Val Gln Gln Gly Lys Ser Gly
225 230 235 240

Thr Phe Asn Val Ser Leu Ser Thr Ala Pro Ala Ser Asn Val Thr Ala
245 250 255

Thr Val Ala Arg Thr Ala Gly Asn Thr Gly Leu Ser Val Thr Gly Gly
260 265 270

Ala Ser Leu Thr Phe Thr Pro Ala Asn Trp Ser Thr Pro Gln Lys Val
275 280 285

Thr Val Ser Ala Asp Gly Ser Gly Thr Gly Ala Ala Thr Phe Thr Val
290 295 300

Ser Ala Pro Gly His Gly Lys Ala Glu Val Thr Val Thr Gln Leu Ala
305 310 315 320

Gly Ala Lys Glu Tyr Asp Ala Arg Phe Leu Asp Leu Tyr Gly Lys Val
325 330 335

Thr Asp Pro Ala Asn Gly Tyr Phe Ser Pro Glu Gly Ile Pro Tyr His
340 345 350

Ser Val Glu Thr Leu Ile Val Glu Ala Pro Asp His Gly His Glu Thr
355 360 365

Thr Ser Glu Ala Tyr Ser Tyr Leu Ile Trp Leu Gln Ala Met Tyr Gly

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    370                 375                 380

Lys Ile Thr Gly Asp Trp Thr Arg Phe Asn Gly Ala Trp Asp Thr Met
385                 390                 395                 400

Glu Thr Tyr Met Ile Pro Thr His Ala Asp Gln Pro Thr Asn Ala Tyr
                405                 410                 415

Tyr Asp Ala Ser Lys Pro Ala Thr Tyr Ala Pro Glu His Asp Thr Pro
            420                 425                 430

Asn Glu Tyr Pro Ala Val Leu Asp Gly Ser Val Ser Ser Gly Ser Asp
        435                 440                 445

Pro Ile Ala Ala Glu Leu Lys Ser Ala Tyr Gly Thr Asp Asp Ile Tyr
    450                 455                 460

Gly Met His Trp Ile Gln Asp Val Asp Asn Val Tyr Gly Tyr Gly Asn
465                 470                 475                 480

Ser Pro Gly Thr Cys Ala Ala Gly Pro Thr Gln Thr Gly Pro Ser Tyr
                485                 490                 495

Ile Asn Thr Phe Gln Arg Gly Pro Gln Glu Ser Val Trp Glu Thr Val
            500                 505                 510

Thr His Pro Thr Cys Asp Asn Phe Thr Tyr Gly Gly Ala Asn Gly Tyr
        515                 520                 525

Leu Asp Leu Phe Thr Gly Asp Ser Ser Tyr Ala Lys Gln Trp Lys Phe
    530                 535                 540

Thr Asn Ala Pro Asp Ala Asp Ala Arg Ala Val Gln Ala Ala Tyr Trp
545                 550                 555                 560

Ala Asp Val Trp Ala Lys Glu Gln Gly Lys Ser Ala Asp Val Ala Gly
                565                 570                 575

Thr Val Gly Lys Ala Ala Lys Met Gly Asp Tyr Leu Arg Tyr Ser Met
            580                 585                 590

Phe Asp Lys Tyr Phe Lys Lys Ile Gly Asp Cys Val Gly Pro Thr Thr
        595                 600                 605

Cys Pro Ala Gly Ser Gly Lys Asp Ser Ser His Tyr Leu Met Ser Trp
    610                 615                 620

Tyr Tyr Ala Trp Gly Gly Ala Thr Asp Thr Ser Ala Gly Trp Ala Trp
625                 630                 635                 640

Arg Ile Gly Ser Ser His Ala His Gly Gly Tyr Gln Asn Pro Met Ala
                645                 650                 655

Ala Tyr Ala Leu Ser Ser Val Ala Asp Leu Lys Pro Lys Ser Ala Thr
            660                 665                 670

Gly Gln Gln Asp Trp Ala Lys Ser Leu Asp Arg Gln Leu Asp Phe Tyr
        675                 680                 685

Gln Trp Leu Gln Ser Asp Glu Gly Ala Ile Ala Gly Gly Ala Thr Asn
    690                 695                 700

Ser Trp Lys Gly Gly Tyr Ala Gln Pro Pro Ala Gly Thr Pro Thr Phe
705                 710                 715                 720

His Gly Met Tyr Tyr Asp Glu Lys Pro Val Tyr His Asp Pro Pro Ser
                725                 730                 735

Asn Gln Trp Phe Gly Phe Gln Ala Trp Ser Met Glu Arg Val Ala Glu
            740                 745                 750

Tyr Tyr His Glu Ser Gly Asp Ala Gln Ala Lys Ala Val Leu Asp Lys
        755                 760                 765

Trp Val Asp Trp Ala Leu Ser Glu Thr Thr Val Asn Pro Asp Gly Thr
    770                 775                 780

Tyr Leu Met Pro Ser Thr Leu Gln Trp Ser Gly Ala Pro Asp Thr Trp
785                 790                 795                 800
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Asn Ala Ser Asn Pro Gly Ser Asn Ala Gly Leu His Val Thr Val Ala
                805                 810                 815

Asp Tyr Thr Asn Asp Val Gly Val Ala Gly Ala Tyr Ala Arg Thr Leu
            820                 825                 830

Thr Tyr Tyr Ala Ala Lys Ser Gly Asp Ala Asp Ala Lys Ala Thr Ala
        835                 840                 845

Glu Ala Leu Leu Asp Gly Met Trp Gln His Tyr Gln Asp Asp Ala Gly
    850                 855                 860

Val Ala Val Pro Glu Thr Arg Ala Asp Tyr Asn Arg Phe Asp Asp Pro
865                 870                 875                 880

Val Tyr Val Pro Gly Gly Trp Thr Gly Ala Met Pro Asn Gly Asp Thr
                885                 890                 895

Val Asp Gln Asp Ser Thr Phe Val Ser Ile Arg Ser Phe Tyr Gln Asp
            900                 905                 910

Asp Pro Asn Trp Pro Lys Val Gln Ala Tyr Leu Asp Gly Gly Ala Ala
        915                 920                 925

Pro Val Phe Thr Tyr His Arg Phe Trp Ala Gln Ala Asp Ile Ala Leu
    930                 935                 940

Ala Leu Gly Ala Tyr Ala Asp Leu Leu Glu
945                 950


<210> SEQ ID NO 17
<211> LENGTH: 360
<212> TYPE: PRT
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 17

Met Ala Gly Arg Ser Arg Leu Ile Ser Leu Ala Ala Val Leu Ala Thr
1               5                   10                  15

Leu Leu Gly Ala Leu Gly Leu Thr Ala Leu Trp Gln Gly Lys Ala Glu
            20                  25                  30

Ala His Gly Val Ala Met Met Pro Gly Ser Arg Thr Tyr Leu Cys Gln
        35                  40                  45

Val Asp Ala Leu Ser Gly Thr Gly Ala Leu Asn Pro Thr Asn Pro Ala
    50                  55                  60

Cys Arg Asp Ala Leu Ser Lys Ser Gly Ala Asn Ala Leu Tyr Asn Trp
65                  70                  75                  80

Phe Ala Val Leu Asp Ser Asn Ala Gly Gly Arg Gly Ala Gly Tyr Val
                85                  90                  95

Pro Asp Gly Thr Leu Cys Ser Ala Gly Asp Arg Ser Pro Tyr Asp Phe
            100                 105                 110

Ser Ala Tyr Asn Ala Ala Arg Ala Asp Trp Pro Lys Thr His Leu Thr
        115                 120                 125

Ser Gly Ala Gly Ile Gln Leu Gln Tyr Ser Asn Trp Ala Ala His Pro
    130                 135                 140

Gly Asp Phe Arg Val Tyr Val Thr Lys Pro Ser Trp Ser Pro Thr Ser
145                 150                 155                 160

Ala Leu Gly Trp Asn Asp Leu Gln Leu Val Gln Thr Val Ser Asn Pro
                165                 170                 175

Pro Gln Gln Gly Ser Pro Gly Ala Asn Gly Gly His Tyr Tyr Trp Asp
            180                 185                 190

Leu Thr Leu Pro Ser Gly Arg Ser Gly Asp Ala Leu Met Phe Ile Gln
        195                 200                 205

Trp Val Arg Ser Asp Ser Gln Glu Asn Phe Phe Ser Cys Ser Asp Ile
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    210                 215                 220

Val Phe Asp Gly Gly Lys Gly Glu Val Thr Gly Ile Gly Gly Ser Gly
225                 230                 235                 240

Asn Gly Thr Pro Thr Pro Thr Pro Thr Pro Thr Pro Thr Asp Pro Glu
                245                 250                 255

His Ser Gly Ser Cys Met Ala Val Tyr Asn Val Glu Ser Ser Trp Asn
            260                 265                 270

Gly Gly Phe Gln Ala Ser Val Glu Val Met Asn His Gly Thr Glu Pro
        275                 280                 285

Arg Asn Gly Trp Ala Val Gln Trp Lys Pro Gly Thr Gly Thr Gln Ile
    290                 295                 300

Asn Ser Val Trp Asn Gly Thr Leu Ser Thr Gly Ser Asp Gly Thr Val
305                 310                 315                 320

Thr Val Arg Asn Val Asp His Asn Arg Val Ile Ala Pro Asp Gly Ser
                325                 330                 335

Val Thr Phe Gly Phe Thr Ala Asn Ser Thr Gly Asn Asp Phe Pro Ala
            340                 345                 350

Gly Thr Ile Gly Cys Val Thr Ser
        355                 360


<210> SEQ ID NO 18
<211> LENGTH: 1089
<212> TYPE: DNA
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 18

atggcccgcc gcagccgact gatctcactt gcagcggtct tggcaacctt gcttggcgca     60

ttgggtctga cggccctgtg gccgggcaag gccgaagcgc atggtgtcgc aatgacaccc    120

ggtagccgga cctacctgtg ccagttggac gccctcagtg ggacaggtgc gcttaacccg    180

acgaaccccg cctgtcgaga tgcactgagc cagtcgggtg ccaacgccct ctataattgg    240

ttcgcagtac tggactctaa cgccggcgga aggggagcgg gctatgtgcc agacggatcc    300

ctgtgcagtg caggggaccg ctccccctac gatttctcag catacaatgc ggcacgtgcc    360

gactggccgc ggacccacct gacgagcggc gccacactca aggtccaata ttcgaactgg    420

gcagcacacc ccggtgactt ccgtgtgtat ctgacaaaac ccggatgggc gccgacctca    480

gagctggcct gggatgacct tcagctcgtg caaaccgtct cgaatccgcc ccaacaagga    540

ggagcaggca ccaacggggg gcactactat tgggatctgg cgctgccgag cgggagaagt    600

ggagacgcat tgatgttcat ccagtgggtg cgttcggata gccaggagaa cttcttctcg    660

tgtagtgata tagtgttcga cggaggtaat ggggaggtaa ctggaatcgg gggaacggga    720

acacccacac cgacccccac gccgaccccc acccctacgc cgacagaccc tgagcatagc    780

ggtagttgca tggcagtcta caacgtggtc agttcatggg ccgggggatt ccaggcaagc    840

gtggaagtca tgaaccacgg cacggagccg cgcaacgggt gggcggttca atggaagccg    900

gggagcggta cccagattaa cagtgtatgg aacggatcgc tgtccaccgg tagcgacggg    960

acggtcacag tgcgggacgt cgaccacaac cgtgtaatcg caccggatgg tagtgtgacg   1020

ttcggtttca ccgccacatc aaccggcaat gactatcccg cagggacgat cggatgcgtg   1080

acctcgtag                                                           1089


<210> SEQ ID NO 19
<211> LENGTH: 2865
<212> TYPE: DNA
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<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 19

atggcagcac ttgcactccc gctggggatg acggccgcag cgggtacgga ggcacaggcc 60

gcagcggtag cctgtagcgt cgattacacc accagcgact ggggcagtgg tttcactaca 120

gagctcacat tgaccaaccg cggaagcgca gccatcgatg gctggacgct tacatacgac 180

tatgcgggta atcagcagct gacgagcgga tggagtggta cctggtccca gagcggcaaa 240

acagtctctg tcaaaaacgc agcctggaat ggagcaattg cggcgggagc agcggtaacg 300

acaggtgccc aattcacgta cagtggagcc aataccgccc cgacaacctt cgcagtaaac 360

ggaaccgtgt gcgccggagc acatcagccg ccaatcgcag tcctgaccag tccggcagcc 420

ggagcagttt tctcggcggg ggatccagtg cccttggcgg cgacagcggc agccgcagac 480

ggtgcaacaa tctcgaaggt cgaattttac gacgacacga cgctgctcgg taccgacaca 540

acatcgccgt acagttatga ggccggacag ctcgccgcag gttctcacag tgtatacgca 600

agagcctacg actctctggg agcctcagca gatagtcctc cggcgggcat aacggtcgtc 660

acaggaccgg cggtcgtagt atcaccagcg cagctgggtg tgcagcaagg taggagcgga 720

acgttcgacg tatccctgag cacggccccc gcagctgacg tgaccgtgac agccgcacgt 780

tcggcaggta atacgggctt gtcggtgacc gggggcagca cgcttacctt cacacccgcc 840

aactggtcga cgccgcaaaa agtgacagtc acagcagacg gatcgggaac gggtgcggca 900

acattcacgg tcactgcacc gggtcacggc aaggcagagg tgaccgtcac gcagctggcg 960

gcagcgaagg agtacgacgc ccgcttcctt gacctctacg gaaaaatcac ggaccccgcg 1020

aacgggtatt tcagcccgga gggtattccc tatcactcgg tggaaacctt gatcgttgaa 1080

gccccggacc acggacatga aaccacgtcg gaagcatatt cctacctgat atggctgcag 1140

gcaatgtatg ggaaaatcac aggagactgg acgaagttca acggagcatg ggataccatg 1200

gaaacgtaca tgatcccgac ccacgcagac caaccgacta atagcttcta tgatgcgagt 1260

aagcccgcaa catacgcccc ggagcacgac acccccaatg aatatccggc agtcctggac 1320

ggttcggcaa gttccggaag cgaccccata gccgcagagc tcaaatcggc atatggtacg 1380

gatgacatct acggcatgca ctggatccag gatgtggaca atgtctatgg ttacggaaac 1440

gccccgggca cctgtgcagc ggggcccaca caggcaggtc caagctacat caacacgttc 1500

caacgggggt cccaggagag cgtatgggag acggtcaccc acccgacatg cgacaatttc 1560

acgtatggag gcgcaaacgg ttacctcgat ctgttcaccg gcgattcgtc gtacgcgaag 1620

cagtggaagt tcacaaatgc cccggacgca gacgcccgcg ccgtgcaagc agcatattgg 1680

gcggacgtgt gggccaagga acaaggcaag gcaggagagg tcgcagacac agtgggaaag 1740

gcagcgaaga tgggtgacta tctgcgctac agcatgttcg acaagtattt caagaagatt 1800

ggcgattgcg taggaccgac cacatgcccc gcaggttcgg gcaaggactc cgcacactat 1860

cttatgagct ggtactatgc atggggcggc gccacggaca cttcggcagg ctggtcctgg 1920

cgcatcggtt ccagccatgc acatggtggc tatcagaacc cgatggcagc gtacgcactg 1980

tcctccgtag cagatctcaa gccgaagagc gccacgggtg cacaagattg ggcaaagagt 2040

ctggaccggc agttggactt ctaccagtgg ctgcagtccg acgagggcgc gatcgcgggg 2100

ggtgcaacca atagctggaa gggatcgtat gcacaaccgc ccgcgggcac gcccaccttc 2160

tatggaatgt actatgacga aaagccggtg tatcacgacc cgccgagcaa ccaatggttc 2220

gggttccagg catggagcat ggagcgagtc gcagaatact accatgagtc gggcgacgca 2280

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caggcaaagg cagtcctgga taagtgggtg gactgggccc tctcagaaac gacagtcaac 2340

cccgacggaa cgtatctcat gcccagcaca ttgcagtggt cgggtgcgcc ggatacatgg 2400

aatgcaagta acccgggtgc aaacgcccaa ctccacgtga ccgtggcaga ctatacagac 2460

gatgtcggcg tggccggggc atacgcccgc acgcttacgt attatgccgc aaaaagcggc 2520

gacacggaag cagaggcgac cgccgaggca ctgctggatg gtatgtggca acatcaccag 2580

gacgacgcgg gtgtggcagt ccccgaaacc cgcgcggact ataatcgatt tgacgatccg 2640

gtgtatgtcc cgggaggttg gactggcgcc atgccgaacg gagacacagt ggatgaggac 2700

agtacgttct tgtcaatccg ttcgttttat aaagacgatc ccaactggcc gcaggtccag 2760

gcatatctgg acggtggtgc cgcaccggtc ttcacttacc atagattctg ggcacaagca 2820

gatattgcac tggccctggg tgcatacgca gacctcctcg aatga 2865

<210> SEQ ID NO 20
<211> LENGTH: 1371
<212> TYPE: DNA
<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 20

atgaagcgct tcctggcact cctcgccacc tgtgcaacgg tcctcgggct gaccgccctt 60

acaggacccc aagcagtagc cgcggcggga tgcaccgccg attataccat aacgtcgcag 120

tggcagggcg gattccaagc agcagtaaaa gtgaccaatc tgggtacacc ggtcaccggt 180

tggaagctca cattcacatt gccggatgca gggcagaaag tggtgcaggg ctggaacgca 240

gcgtggagcc aatcgggatc ggcggtgaca gccgcagggg ccgactggaa tggtaccctt 300

gcaaccggtg cgagtgcaga ggcgggcttc gtcggttcgt tcacaggggc caacccgcca 360

ccgacagcgt tcgcactcaa tggagtcgcc tgtaccggtt caaccggtga gccaccggcg 420

ggaagcgatg gcggcacacc ggtcgatgta aacggtcagc tccatgtatg tggagtcaac 480

ctgtgtaacc agtacgaccg tccagtgcaa ttgcgcggta tgtccaccca cggtatccag 540

tggttcgacg catgctatga cgcggcaagt ctggacgcgc tggccaacga ctggaagtcc 600

gacctcctgc gaattgcaat gtatgtgcag gaagacggat acgagacaga cccggccgga 660

ttcacgcgtc gggtcaatga cctggtagac atggcagaag cccgcggcat gtatgccctg 720

atagatttcc acacgctgac tcccggtgac ccgaatgtca accttgatcg tgccaagacc 780

ttcttcgcga gcgtggccgc aagaaatgcc ggtaaaaaga acgtcatcta tgagatcgca 840

aacgagccga acggagtaac ctggacagca gtcaagtcgt atgccgagca ggtgataccc 900

gtcatccgcg cagcagaccc ggacgcagtg gtaatcgtgg gaaccagggg ttggagcagt 960

ctcggtgtca gcgacggatc ggacgagagt gaagtggtca acagtccggt gaatgccacc 1020

aacattatgt acgcattcca cttttatgcc gcgagccaca aagacgcgta cagaagtacg 1080

ctcagcaggg cggcagcacg tcttcccctg ttcgtcacag aattcggtac cgtaagtgcc 1140

accggtggag gagccatgga tcgggcaagc accaccgcgt ggctggacct gctcgatcag 1200

ctcaaaatct cgtatgcaaa ctggacatac agtgacgcac cggagagctc cgcggccttc 1260

cgcccgggga cctgtggtgg aggtgactat tccggatcag gtgtattgac ggagagcggc 1320

gcacttctca agaatcgtat aagtacaccg gattcattcc cgactggtta a 1371

<210> SEQ ID NO 21
<211> LENGTH: 2730
<212> TYPE: DNA

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<213> ORGANISM: Streptomyces sp SirexAA-E

<400> SEQUENCE: 21

atgtggtgcc acccctacct gcgtctccgc accagcggac gaaaggtatc cagtgtaaat 60

gctttgcctc ccccagcacg tcctgcacct gtgcggccac ggtcccggta cggtcgccgg 120

gtcctcggaa tgtcggcggc cgcactcctg tgtgccggag cactcgcagt accgggtaca 180

gcgatggcag atgatgccga accggggccg ggtccagagc agatcacgaa cggtgacttc 240

gccaccggaa cgtcggcacc gtggtggtgg acgcccaacg cgtccgcagc cgtgtcggaa 300

ggtcgtctgt gcgtagaggt gccggcaggc acggccaatg catgggatgt aatagtcggc 360

cagaacgacg tacccatcgt cgcgggtgaa agttacgagc tcagttacac cgcccgctcg 420

acagtcccgc tcacggtgca aacccgggtc caagaggcag tggagccgta caccacggta 480

ctggccaccg cagaccccgt aggtgcggag gatacacgcg tggcacgcac gttcacggcg 540

tccgtcgacc aaccggcggc atcagtacag ctgcagatag gcggaggaga acgggcaacc 600

accttctgtt tggacgacgt gtctctgcgc ggaggcgcag agcccccggt gtatgtcccg 660

gatacaggga gtccggtgcg cgtgaaccag gtaggttacc ttcccagggg accaaagtcg 720

ggcacagtgg tcaccgacgc agaagcgccc ctgacgtgga ccgtgaaggc agaggacggt 780

tcgaccgcgg ccaccggtac gaccgtcccg cggggagaag acccgagctc gcgccgacgt 840

gtgcacacat tcgatttcgg tgacctcacc acagccggcg acggatatac cgtagaggtc 900

gacggtgagg taagcgagcc cttctcaatt cgcggtgatc tgtacgactc gctgcgtagc 960

gacgccctcg cgtatttcta tcataaccga tcgggaatcg agatcgacgc cgacctggtc 1020

ggggagcaat acgcacgtcc cgcaggtcac attggcgtcg caccgaataa gggagacacc 1080

gacgtcccgt gtcgccctgg agtgtgtgat taccgcctcg acgtctccgg gggatggtac 1140

gacgcgggcg atcacgggaa atatgtagtg aacggaggta tcagcgtggc ccagcttatg 1200

gcaacgtacg aacgtaccct cacggcgccg gatgcggagt cggccgaact cggagatggt 1260

gcactccgcg tcccggagcg cgacaatgga gtgcctgaca ttttggacga agcacggtgg 1320

gagatggatt tcctgatcaa gatgcaggta ccggctggcg aacaactcgc aggcatggtg 1380

caccacaaaa tgcacgacgc cgaatggacc ggactcccaa tgaagcccca tctcgacccc 1440

cagcagcgcg agctgcatcc tccgtccacg gcagcaacac tcaatttggc agccaccgca 1500

gcacagtgtg cacgtctgta tgccccattc gacgcagact tcgccgatcg ctgtctgagg 1560

gccgcagaaa ccgcctggga cgcagccaaa aggcacccgg acgtcctcgc agatcccaac 1620

gacggaatcg gtggcggtgc atataatgac gacgatgtat cagacgagtt ctactgggca 1680

gcggccgagt tgttcaccac gacagggaag gatatttacc gtcaggcggt cttgtcgagc 1740

gcctggcatg gagacgcagg tgccgtattc ccggcgggcg gaggtatctc gtggggtagc 1800

acggcaggcc tcggtgtcct taccctggca acagtcccca acgctttgac ctcggatcag 1860

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gcgcaccaaa acgatccgtc gttgcccaac ccggcccccg gctcgattgc cggcggaccc 2220

aacctcacag caatcgcaag tggcgatccc gtagcagcgg agaagctgag cggttgtgca 2280

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cccgcaatgt gctacgtgga cgatattgga agttgggcaa ccaacgaaat cacgatcaac   2340

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acagccgcag cccgcacgtg ccaagtcacc tattcgagcc acccgtggaa cagtggatca   2460

acagtaacgg tccgtgtgga gaataccggt tcggatccgg tgtcgccctg ggccctcacg   2520

tggttgctgc cgggggaaca gcgcctcagt cacacttggt cagccgagtt cgaccaacat   2580

ggccgtacgg tcagcgcacg ccccctgtcg tggaatcgta cactggcacc gggagcggca   2640

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ctcaacggaa gggcatgtag cgcaggttga                                    2730


<210> SEQ ID NO 22
<211> LENGTH: 1752
<212> TYPE: DNA
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 22

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gccctcgtag cagcagcagc gggcagtgca gccgcagccg caccttttcgc agcgtccgca    120

gcagccgcaa ccggatgcac cgtagactat aaaatcgaga accagtggaa cggaggactg    180

acagccgcag tcaacgtcac caacaacggc gcgccggtaa cgtcatggca gctgcagtgg    240

accttcaatg ggggagaaca agtctcccag ggatggaacg caacaatcag ccagagcggg    300

tcagcagtaa ctgcaaaaga tgccggttac aatggtacac tggcaacagg cgccagcgca    360

tcgtttggat tcaacgccac aggtaatggc aacagtaccg tcccggcgac attcaaactg    420

aacggagtga cctgtaacgg ggataccacc ggacccacag acccaacgga tcctacggac    480

ccgacggatc ccccggcagg gaatcgcgtg gacaacccgt atcagggcgc aaaggtatac    540

gtgaatccgg agtggagcgc gaacgccgca gcggaacctg ggggttcccg tgtcgcaaac    600

caacccaccg gagtgtggct cgaccgcata gcagcgatcg agggtgccaa tggatcgatg    660

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ctcggaccga cagaaatcgg cagatataag accgagtaca tcgacccaat cgcggccata    840

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cctaatctgg taacgaacgc aggtggccgt gaaaccgcaa caccggcatg tgatgtcatg    960

aaggcaaacg gaaactatgt caagggcgtg ggatatgcac tgaacaagct cggagacgcg   1020

cccaatgtct acaactatat tgacgccggt caccacggat ggatcgggtg ggacgataat   1080

ttcggcgcat cggcgcaaat attccacgaa gcagcaactg cggagggagc aaccgtaaac   1140

gacgtgcacg gtttcatcac gaacacggcg aattacagcg cactgaaaga acagaacttc   1200

agcatcaacg atagcgtcaa tggcacttcc gtgagggaat cgaagtgggt cgactggaac   1260

cgctacacgg acgagctcag cttcgcacaa gcgttccgga acgaacttgt gagcgtcggc   1320

ttcaattcgg gtattgggat gctgatcgac accagtcgaa acggctgggg aggtagcgca   1380

cggcccagtg gaccaggggc taccaccagt gtcgacacgt atgtggatgg tggccgctat   1440

gaccggcgca tccacctggg aaactggtgc aatcaagccg gagcaggttt gggggaacga   1500

ccaaccgcag cccccgagcc cggtatcgac gcatatgttt ggatgaagcc gccgggagag   1560

tcggacgggt ccagctccga gatccctaat gatgagggta aaggcttcga ccgcatgtgt   1620
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gacccgacat acacgggaaa cccccggaac aacaacaatc cgtcgggcgc attgggggga 1680

gcgcccgtga gtggtaagtg gttctcggcc cagttccagg agctcatgaa gaacgcatat 1740

cctgcactct ga 1752

<210> SEQ ID NO 23
<211> LENGTH: 1083
<212> TYPE: DNA
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 23

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ctgggcctca ccgccctctg gcagggtaag gcggaagcac atggggtcgc aatgatgccc 120

ggaagccgga catatctgtg ccaagtggac gccctctctg gcaccggagc actgaacccg 180

acaaacccgg catgtcgcga tgcgctgagc aaatcgggtg caaatgccct gtacaattgg 240

ttcgcagtcc tggacagtaa cgccggcgga agaggtgcag gctacgtgcc ggatgggacc 300

ctgtgctccg ccggcgacag aagcccgtac gacttcagcg catataatgc ggcacgtgcc 360

gactggccga agacgcacct gacgagtggc gcaggaatcc agttgcagta tagcaattgg 420

gccgcacatc cgggcgactt ccgagtctac gtcactaagc cgtcgtggtc acccacaagc 480

gcgctcggat ggaacgacct gcagctggta cagaccgtgt cgaatccgcc gcagcagggc 540

agccctggag ccaacggtgg tcactattat tgggacctca ccctgccgtc gggtcggtcg 600

ggggacgcac tgatgttcat ccagtgggtc cgtagcgaca gtcaggagaa cttcttctcc 660

tgttcggaca tagtattcga cggaggcaag ggcgaagtga ccggtatcgg ggggtccggt 720

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ggtacgcaga tcaacagtgt atggaacggt accctgtcca cagggtcgga cggtaccgtc 960

acagtcagga acgtggacca taaccgcgta atagcaccgg atggaagcgt cactttcggc 1020

ttcaccgcca attcgacagg aaacgacttc cccgcgggca cgatcggatg tgtaacgagt 1080

tga 1083

<210> SEQ ID NO 24
<211> LENGTH: 2865
<212> TYPE: DNA
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 24

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gcagcggtag catgctcagt agactacaag gccaacgatt ggggttcggg cttcaccacc 120

gaactgacac tcacaaatcg cggtagtggt gcgatcgacg gatggacact cacgtacgat 180

tatgccggta accagcagtt gacatcagga tggtcgggtg tgtggagtca gagtggtaag 240

acggtaacag tgaagaacgc agactggaac ggaaccgtcg cggccggcca ggcagtcaca 300

gccggtgcac agttcacgta tagtggaacc aatacagacc cgacagcgtt cgcagtgaac 360

gggaccgtat gcgcgggagc acaccagccc ccgatagccg tcctcaccag ccctgcagca 420

ggagcggtct tcacagcagg cgatccggta ccgctggccg caaccgcagc agcagcggac 480

ggtgcgacca tttccaaggt ggagttctac gacaacacta cactgctcgg cacagacact 540

acctcaccat actcatatac agcgcaagga ctgtcagccg ggagtcattc cgtgtatgca 600

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cgcgcatacg actcattggg tgcgagcgca gaaagtccgc cagccggaat caccgtcgca 660

gcgggtccgg cagtagtcgc aacacccgcc cagctcggag tacagcaggg aaagtcgggc 720

accttcaacg tgtccctttc aactgcaccg gcctcaaatg tcacagcaac cgtcgcacgg 780

acggcaggaa atacaggatt gagcgtcacc ggaggcgcgt cactgacctt cacgcccgcc 840

aactggtcga cccctcaaaa agtaaccgtc tccgcagatg gttcgggaac aggagcagca 900

acgttcacag tgagtgcgcc tggtcacgga aaggcagagg taacggtaac gcagctcgcg 960

ggtgcaaagg agtatgatgc acgattcctg gacttgtacg gcaaagtgac cgatccggcc 1020

aacgggtact tctctccgga gggaatacca taccactcag tggagacgct gattgtcgaa 1080

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gaaacctata tgatccccac acacgcagac cagccgacca atgcatatta cgacgccagt 1260

aagcctgcaa catacgcacc cgagcacgac accccaaacg aatacccggc ggtacttgac 1320

ggaagcgtat catcgggctc agaccccatc gccgccgagc tgaagtcggc atatggaacc 1380

gatgacatct atggaatgca ctggatccag gatgtcgaca acgtatacgg ctacgggaac 1440

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cgtataggaa gttcacacgc acacggcggt taccaaaacc ctatggcagc gtatgcgttg 1980

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gcctaccttg acggtggagc ggcgccggtc ttcacgtacc accgtttttg ggcccaggca 2820

gatatcgctt tggccttggg tgcctatgca gacctgctcg aatga 2865

<210> SEQ ID NO 25

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<211> LENGTH: 1140
<212> TYPE: DNA
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 25

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atctgtggcc agtatggaac gacggtaatc caagaccgct atgtcgtcca aaacaaccga 180

tggggaacca cggacgcgca gtgtgtggac gtgaccgacg atgggttcac cgtaacgcgc 240

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tggttcaatc gggtggggcc catacagccg gtcggtagcc agacgggtac cgccacggtg 540

gcaggtagag ggtgggaagt ctggaccggt aacaacggag gtaatgacgt catttccttc 600

gtatccccgt cggcaatctc cagctggagt ttcgacgtca tggacttcgt agacgcaacg 660

gtggcgcgcg gaatggcaca gaactcatgg tatctgacct cggtgcaggc gggcttcgaa 720

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acagtgccag tctcgggatg gcggttgggt ttcacactgc cccaggggca gacggtcacc 960

caggcatgga acgccacggt aaccccgtcg agtggagcag tgacggccac cggtgcagcg 1020

ttcaacgcag agatagcagc aggggcaagt cagagtttcg gatttcaagg tacccactcg 1080

ggaaccttca caaagcccga ccgtttcacc ctcaacggtg cggtctgtac agtcggctga 1140

<210> SEQ ID NO 26
<211> LENGTH: 2667
<212> TYPE: DNA
<213> ORGANISM: Streptomyces DpondAA-B6

<400> SEQUENCE: 26

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gtaccgctca ccgtgcagac gcgcgtccag gaagcagtag agccatacgg aactgtgctc 420

gccaccgcag atccggtcgg aacggaggat acccaggtga cacgtacctt cacagcatcc 480

gtcgatcaac cggcggccag cgtccagctc caaattgggg ggggagaacg cgcgacgacc 540

ttctgccttg acgacgtcag cctccgtggc ggagcagagc ctcccgtata tgtgccggac 600

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cacaaaatgc acgacgccga gtggaccgga ctgccgatga agccgcactt ggacccgcaa 1380

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gccgaactct tcaccaccac aggcaaggac acctatcgtc aagaggtgtt gtcgagtgat 1680

cttcacggtg atgcagatgc cgtcttcccc gcaggaggcg gcctcagctg gggtgccaca 1740

gcagggctcg gggcgctcac actggccacg gtaccgaaca acctgaccac ggaccagctc 1800

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ttgctgccgg gcgagcagaa gctctcccac acctggtcag ccgaattcga gcaacacggg 2520

cgcaccgtgt cagcaaggcc gctggcgtgg aaccggaccc ttgcaccggg agccgcagta 2580

gacttcggct tcaatacgag cgcgacagga gcagcggccg atccaggcac gttcaagttg 2640

aacggtcgcg cctgtgcatc gggctga 2667

<210> SEQ ID NO 27
<211> LENGTH: 2133
<212> TYPE: DNA
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 27

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cgagtcgata atccatatgt cggtgcaaag gcatacgtga acccagactg gagtgcaaaa 180

gcagcggccg aaccgggcgg agcagcgatt gccgatacac cggcgttcgt gtggatggac 240

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cgcatcgcag caatcggtgg tacaccgggt gccatgtcgc tcagggaaca cctggacacg 300

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tgcgcagccc ttgcaagtaa tggggagctg ggaccgacgg agctcgatag gtataagtcc 420

gaatacatcg acccgatcag tgagatcctc gcggacccgg catacgcgaa tctgcggata 480

gtcacaatca tcgagcccga ctcgctgccg aatattgtga cgaatgcggg tggcaccgca 540

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tatgcactcc acaccctcgg tgccatcccg aatgtatata actacgtgga cgcagcccac 660

cacggctggt tggggtggga tagcaacatg gtgccggccg gggtggagtt caagaaggca 720

gcaacaagtg agggagcaac cgtggacgat gtcgcaggat tcatagtaaa tacggcgaac 780

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gcacgcaatg gatggggagg ctcggatcgt ccgacatcag cagggccgct gacgtcggtc 1020

gacgactacg tcaacggtgg ccgggtcgat cgccggatcc atgcgggaaa ctggtgcaat 1080

cagtctggcg caggaatcgg cgagaggccg acctcagcgc ccgaagcggg aatcgacgcg 1140

tatgtatggg caaagccccc cggcgagtcg gacgggagta gtcaggcaga agataacgac 1200

gagggaaaag gtttcgatcg aatgtgtgac ccgacatatg aaggcaacgg aaggaacgga 1260

aacagcaaga cgggcgcgtt gccgaattcc ccagtagcag ggcactggtt cagtgcacag 1320

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gggaacgtgt cggcagcatc gtcagcactg agcgtcacaa cgtcagccgg gggaggcaca 1680

ggaacgggaa gcctgaaggt ccaatataaa aataacgaca acagtccgac agacaaccag 1740

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aagctccgct actggttcac cccagaatcc ggcagctcca cgttcgggac agcctgcgat 1860

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acgggggaaa tgcagctgcg actgaacaag agcgattggt cgaacttcaa tgaggcggac 2040

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<212> TYPE: DNA
<213> ORGANISM: Streptomyces LaPpAH-95

<400> SEQUENCE: 32

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We claim:

1. A heterologous gene cassette for expression in a *Streptomyces* species to enhance growth on a cellulosic polysaccharide substrate, the cassette comprising a glycoside hydrolase family 9 (GH9) endoglucanase gene from *Streptomyces* LaPpAH-95, a glycoside hydrolase family 12 (GH12) endoglucanase gene from *Streptomyces* DpondAA-B6, and at least two four genes selected from the group consisting of:

a) a glycoside hydrolase family 6 (GH6) gene,

b) an auxiliary activity family 10 (AA10) gene,

c) a glycoside hydrolase family 48 (GH48) gene, and

d) a glycoside hydrolase family 5 (GH5) gene.

2. The cassette of claim **1**, wherein the genes are under the control of a single constitutive promoter.

3. The cassette of claim **1**, wherein the genes have been modified to substantially optimize enzyme expression compared to the wild-type sequences.

4. A *Streptomyces* strain recombinantly engineered with the cassette of claim **1**.

5. The strain of claim 4, wherein the *Streptomyces* is selected from the group of *S. lividans* or *S. venezuelae.*

6. A method of digesting a cellulosic polysaccharide comprising the step of exposing a cellulosic polysaccharide substrate to the strain of claim 4 or its secreted products.

7. The method of claim 6 wherein the polysaccharide substrate is selected from the group consisting of miscanthus, switchgrass, hemp, corn, poplar, willow, paper, wood waste, corn stover, prickly pear cactus cladodes, kelp, sorghum, straw, eucalyptus, pine, sugarcane bagasse, cotton, bamboo, nut shells, bark, sawdust, wood chips, and paper mill waste.

8. The cassette of claim 1, wherein the cassette comprises the GH6 gene, the AA10 gene, the GH48 gene, the GH5 gene, the GH9 gene, and the GH12 gene under the control of a single constitutive promoter and each separated by a ribosomal binding site.

9. The cassette of claim 8, wherein the GH6 gene, the AA10 gene, the GH48 gene, the GH5 gene, and the GH12 gene are from *Streptomyces* DpondAA-E36.

10. The cassette of claim 8, wherein the GH6 gene, the AA10 gene, the GH48 gene, the GH5 gene, and the GH9 gene, are from *Streptomyces* LaPpAh-95.

11. The cassette of claim 8, wherein the GH6 gene, the AA10 gene, the GH48 gene, and the GH5 gene, are from *Streptomyces* sp SirexAA-E.

12. The method of claim 6, wherein the cellulosic polysaccharide substrate is selected from the group of cellulose and hemicelluloses.

13. The method of claim 6, wherein the cellulosic polysaccharide substrate is selected from the group of wood and non-wood biomass.

14. The method of claim 6, wherein the cellulosic polysaccharide substrate is a lignocellulosic material.

15. A heterologous gene cassette for expression in a *Streptomyces* species to enhance growth on a cellulosic polysaccharide substrate, the cassette comprising a GH9 endoglucanase gene from *Streptomyces* LaPpAH-95 and at least three genes selected from the group consisting of:

a) a glycoside hydrolase family 6 (GH6) gene,

b) an auxiliary activity family 10 (AA10) gene,

c) a glycoside hydrolase family 48 (GH48) gene,

d) a glycoside hydrolase family 5 (GH5) gene, and

e) a glycoside hydrolase family 12 (GH12) gene.

16. The cassette of claim 15, wherein the cassette comprises the GH6 gene, the AA10 gene, the GH48 gene, the GH5 gene, and the GH9 gene under the control of a single constitutive promoter and each separated by a ribosomal binding site.

17. The cassette of claim 16, wherein the cassette additionally comprises the GH12 gene.

18. The cassette of claim 16, wherein the GH6 gene, the AA10 gene, the GH48 gene, and the GH5 gene are from *Streptomyces* sp SirexAA-E.

19. The cassette of claim 16, wherein the GH6 gene, the AA10 gene, the GH48 gene, and the GH5 gene are from *Streptomyces* DpondAA-86.

20. A heterologous gene cassette for expression in a *Streptomyces* species to enhance growth on a cellulosic polysaccharide substrate, the cassette under the control of a single constitutive promoter and comprising a GH6 gene, a AA10 gene, a GH48 gene, a GH9 gene, and a GH12 gene each from *Streptomyces* LaPpAH-95 and each separated by a ribosomal binding site.

* * * * *